

THE STUDY OF PHOTOCHEMICAL INTERCONVERSIONS
OF SESQUITERPENOIDS RELATED TO α - AND β -VETIVONE

A THESIS

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By

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
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THE STUDY OF PHOTOCHEMICAL INTERCONVERSIONS
OF SESQUITERPENOIDS RELATED TO α - AND β -VETIVONE


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GLOSSARY OF ABBREVIATIONS

Anal	C, H analysis
bp	Boiling point
cm ⁻¹	Wave number (ir spectrum)
DDHQ	2,3-Dicyano-5,6-dichlorobenzohydroquinone
DDQ	2,3-Dicyano-5,6-dichlorobenzoquinone
Hz	Hertz
ir	Infrared
J	Coupling constant
mp	Melting point
nm	Nanometer
nmr	Nuclear magnetic resonance
uv	Ultraviolet
ϵ	Extinction coefficient
δ	Part per million

SUMMARY

One of the purposes of this research was to study the photochemical behavior of the C-4 substituted cross-conjugated cyclohexadienones such as 52, 29 and 32. The primary goal was set on the isolation of the spiro dienones such as 54, 34 and 38 as photochemical intermediates. The skeleton change from 6/6-fused structure to spiro[4.5] structure offered the possibility of interconverting the naturally occurring sesquiterpenes α -vetivone and β -vetivone.

Model compounds 50 and 51 were prepared and oxidized to the corresponding dienone 52. Irradiation of this dienone 52 at 2537 Å in dioxane gave lumipproduct 53 which on irradiation with a broad spectrum lamp in 45 percent aqueous acetic acid gave the spiro dienone 54.

Nootkatone was successfully converted to α -vetivone by two methods. Dehydronootkatone 32 was prepared by oxidation of nootkatone with DDQ and it was isomerized to dehydro- α -vetivone 29 via the method of hydrobromination then dehydrobromination. By irradiation first in dioxane at 2537 Å and then in aqueous acetic acid with a broad spectrum lamp, 29 gave lumipproduct 33 and then spirodienone 34, while 32 gave lumipproduct 36 and then spirodienone 38 along with two other dienones 32 and 37. Trienones 32, 37 and 38 were found to be converted into mixture of approximately the same composition when any one of them was irradiated in 45 percent acetic acid for extended periods.

Hydrogenation of 38 gave a mixture of β -vetivone (28) and its 10-epimer 35 in a ratio of ca. 7:3 while chemical reduction of 38 with lithium in ammonia gave a mixture of 28 and 35 in a ratio of 3:7. Hydrogenation of 29 did not give the desired compound 27 while chemical reduction with lithium in ammonia gave the phenolic compound 60 exclusively.

The course of acid-catalyzed opening of the cyclopropane ring of several bicyclo[3.1.0]hexanone derivatives was also investigated. Dihydrolumiproducs 47, 48 and 49 which were prepared via hydrogenation of their corresponding lumiproducs 62, 53 and 66. Hydrobromination and then dehydrobromination of 47, 48 and 49 was found to give 70, 68 and 72 as major products, respectively. Boron trifluoride etherate treatment of 48 gave 50 as the sole product while treatment of 49 with boron trifluoride under various conditions gave mixtures of four products identified as 72, 73, 74 and 75.

CHAPTER I

INTRODUCTION

Since the careful work on the photochemical rearrangement of α -santonin (1,2,3), the field of research on the photochemical behavior of cross-conjugated cyclohexadienones has been very active (4). With cumulative knowledge, the various products obtained in these reactions were rationalized by such factors as the structural, solvent or light wavelength effects.

In aqueous acid media cross-conjugated cyclohexadienones of type 1 are converted principally to one or more hydroxy ketone photo-products. The general mechanism suggested (5) is first a $n \rightarrow \pi^*$ electron transition to the singlet excited state of the dienone and then intersystem crossing to give the triplet excited state. This is followed by 4,8a-bonding to give a diradical which can be represented by resonance forms 2 and 3. Electron demotion $\pi^* \rightarrow n$ and protonation results in the mesoionic species represented by 4 and 5 (Chart 1). The electronic character of each substituent R_1 and R_2 determines which resonance form is more stable and is important in determining the product composition. Kropp (6a) and also Caine and Dawson (6b), reported the study of 1- and 3-methyl substituted dienones 1a and 1b (Chart 1). The formation of a 5/7-fused hydroxy ketone 6a from 1a and spiro ketone 7b from 1b as the major products appears to be the effect of the methyl substituent. The nucleophilic attack by solvent on the

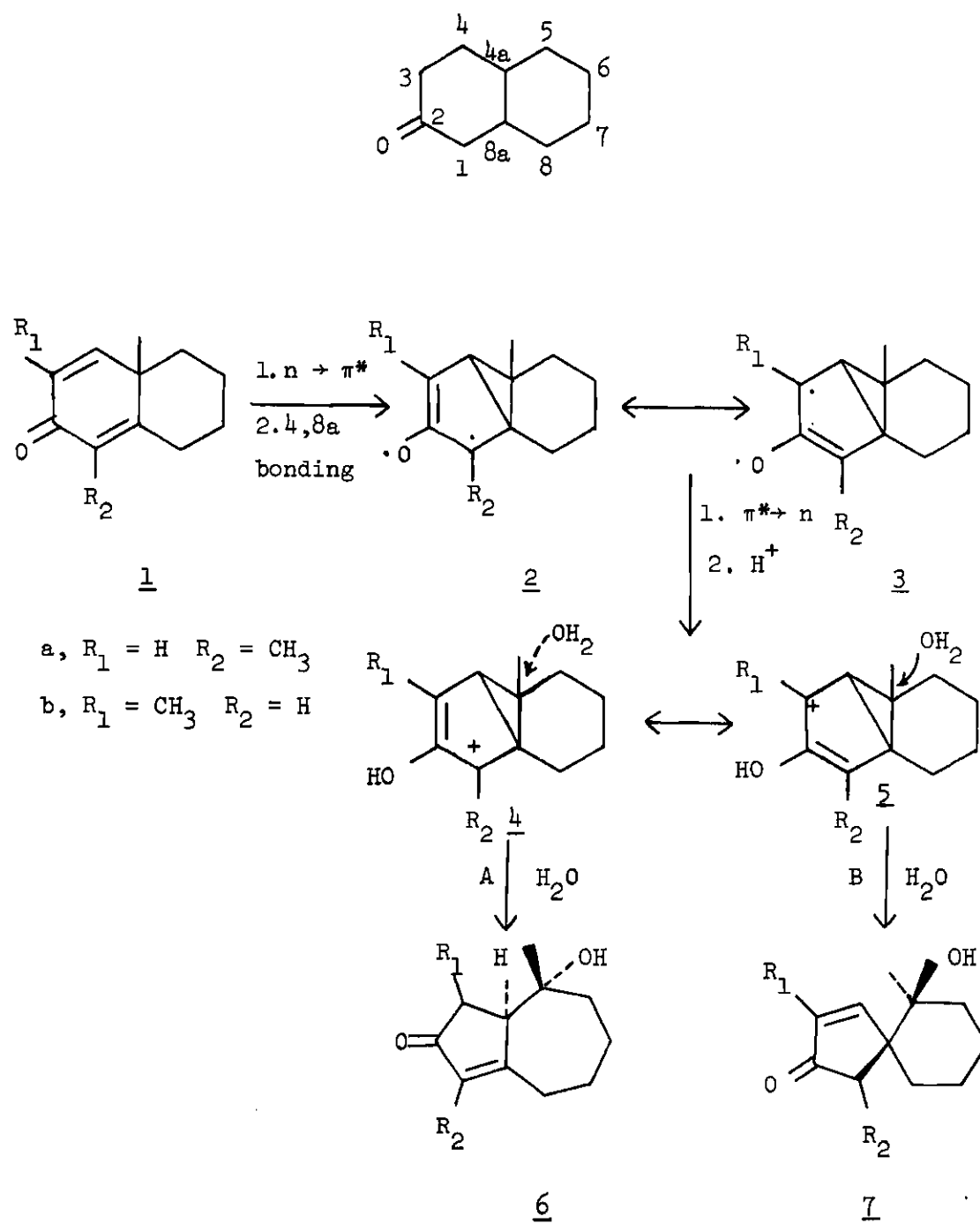
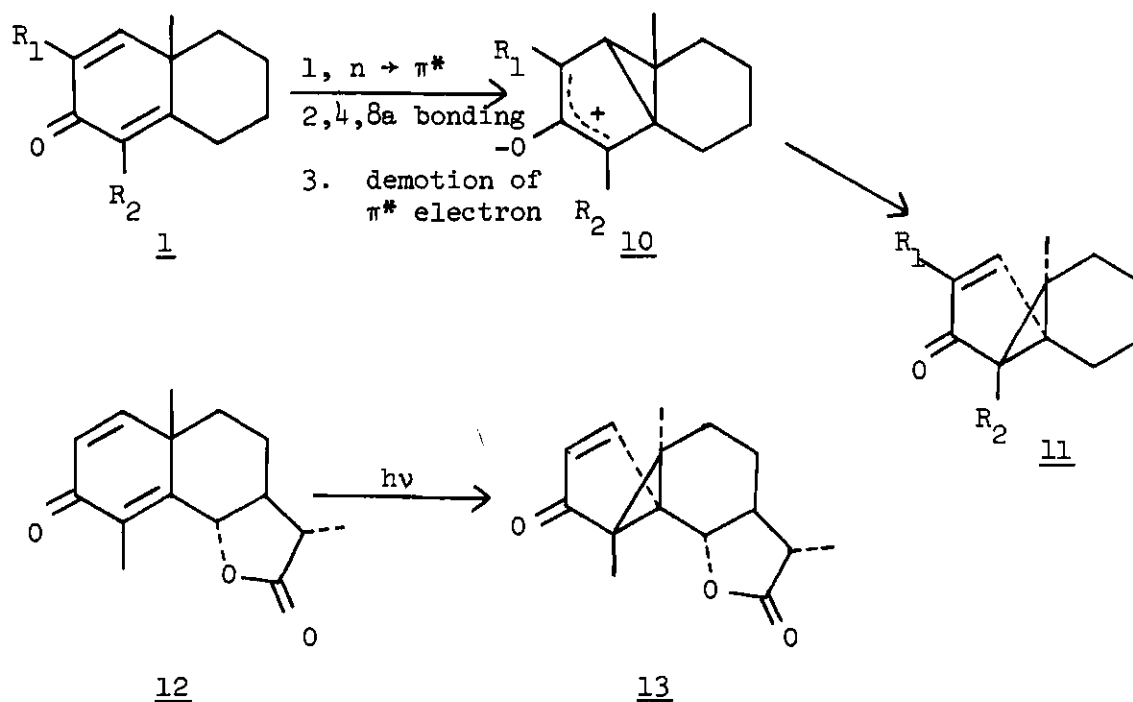


Chart 1 Mechanism of Photochemical Rearrangements of Cross-Conjugated Cyclohexadienones to Hydroxy Ketones



from many unsubstituted or 2-methyl dienones are quite low in the presence of the broad spectrum of a high pressure mercury arc, the difficulty can be overcome by the use of monochromatic light source of 2537 Å. This kind of light source is readily available from a low pressure mercury resonance lamp (6). At this particular wavelength, absorption by the lumiprodut is only about one-sixth that of starting dienone, so that the rate of further conversion of the lumiprodut to its secondary photoproducts is significantly reduced.

The possibility of a four step process which involves spirodienone 14 as an intermediate in the rearrangement of the dienone 1b (see Chart 2) through cyclopropyl ketones 14b and 15 to the linearly conjugated isomer 16 was suggested by Kropp (8). The spirodienone 14 was prepared by solvolysis of the tosylate 17 and

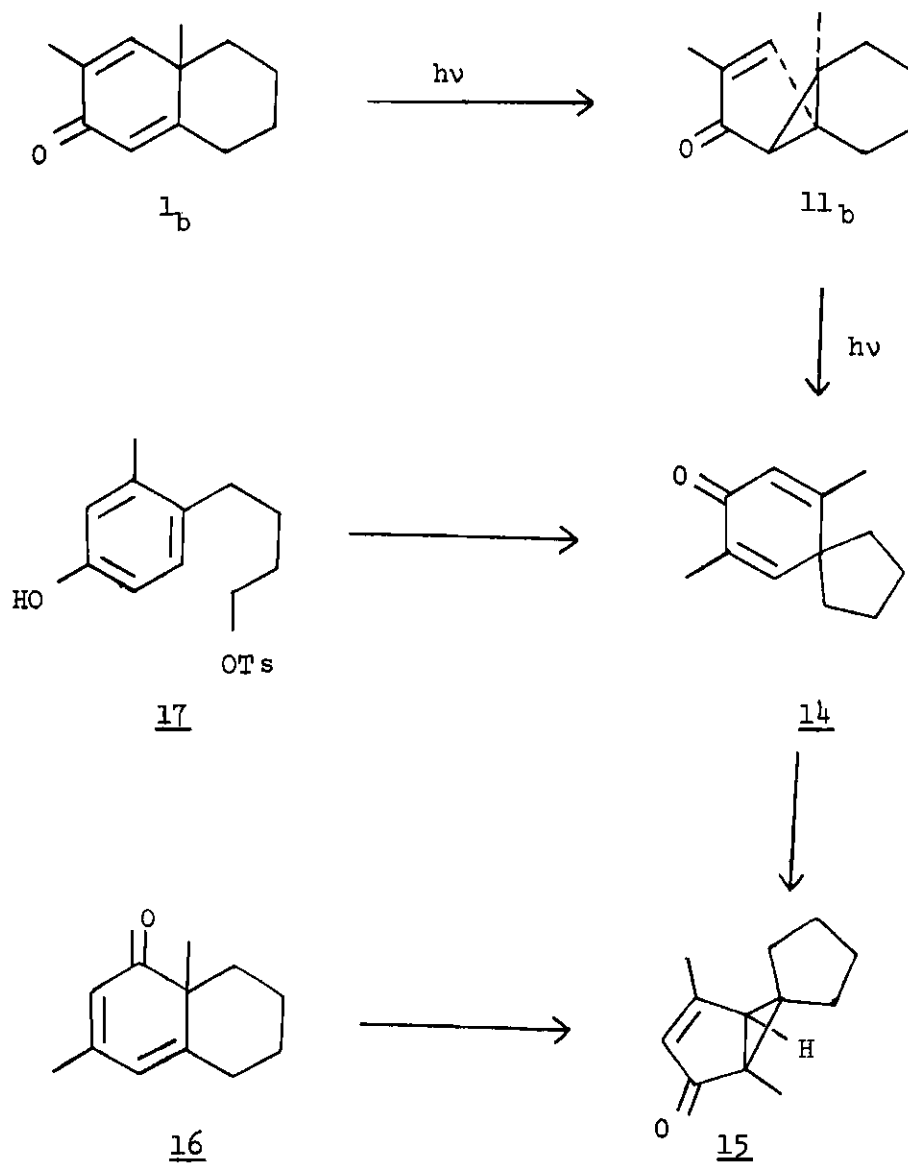


Chart 2 Rearrangement of a 3-Methyl Substituted Dienone

converted principally to the cyclopropyl ketone 15 on irradiation in methanol or dioxane. This cyclopropyl ketone 15, in turn, underwent further rearrangement to the dienone 16.

It has also been found (9) that the unsubstituted analog 18, obtained from the corresponding tosylate 19, gives a mixture of the tetrahydronaphthols 20 and 21 upon irradiation in a variety of solvents (Chart 3).

The actual isolation of spiro dienone intermediates was achieved in related steroidal systems (10). Ultraviolet irradiation of 1-dehydrotestosterone acetate (22a), its 10 α -stereoisomer 23, and its 1- and 4-methyl homologs 22b and 22c in dioxane solution gave the spiro dienones 24a, 24b and 24c as the second intermediate in each reaction; however, in each case the yield of the product 24 was quite low.

Although the intervention of spiro dienone intermediate was quite reasonable, all attempts to isolate or intercept 14 were unsuccessful (8). One of the aims of this research was to find proper controllable conditions which would allow to the isolation or interception of spiro dienones of this type.

The naturally occurring sesquiterpenoids α -vetivone and β -vetivone have long been regarded as isomeric hydroazulenones 25 and 26 (11). However, the recent detailed studies of Marshall and coworkers (11) revealed the correct structures of these compounds as 27 and 28, respectively.

Earlier workers (6) showed interest in investigating and

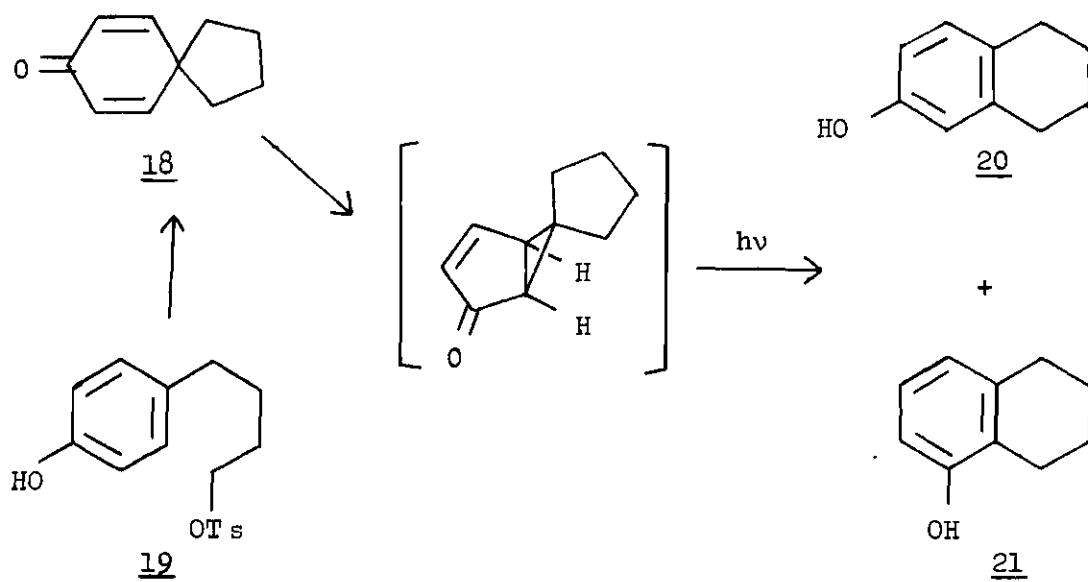
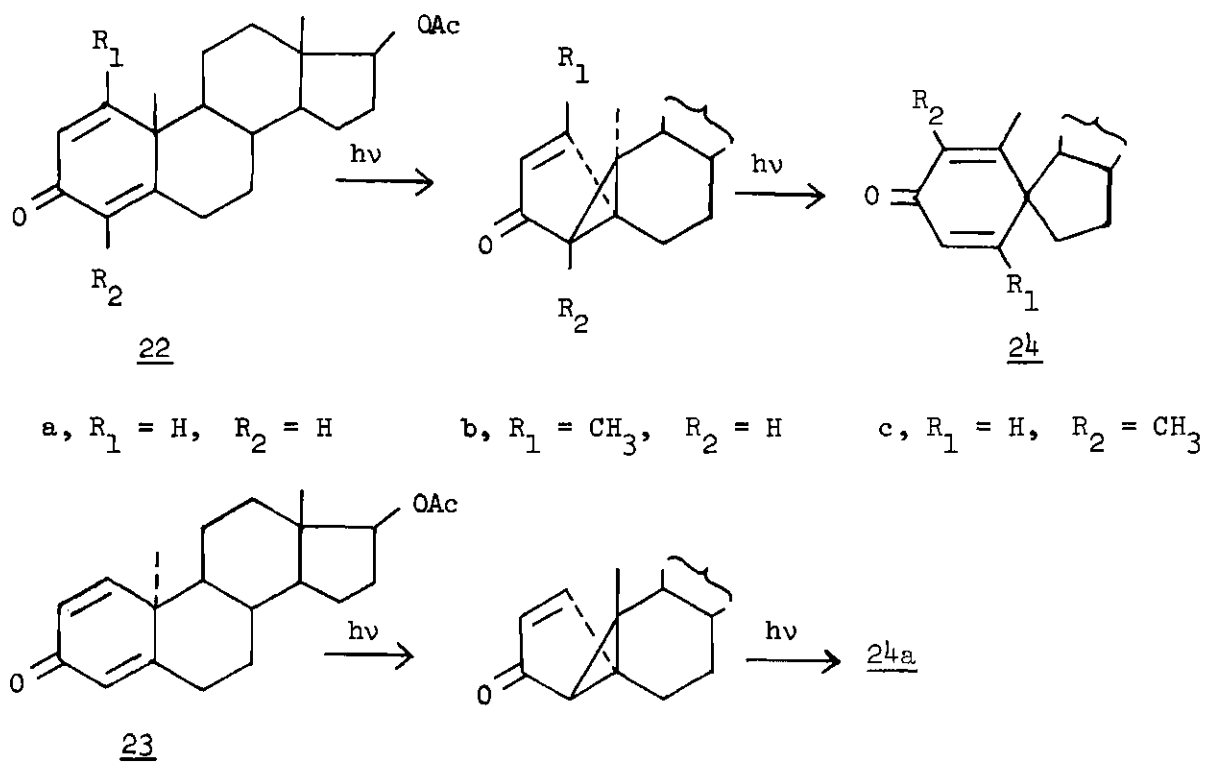
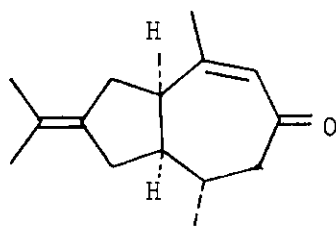
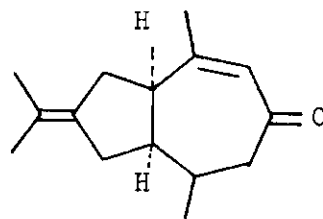
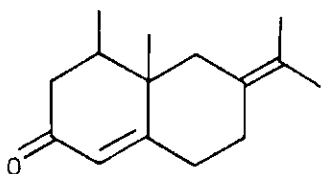
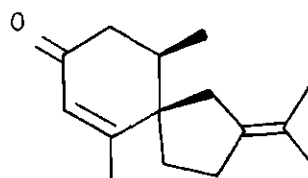


Chart 3. Synthesis and Photolysis of Spiro dienone 18



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comparing the photochemical behavior of 4-methyl substituted cross-conjugated dienones such as dehydro- α -vetivone 29 with that of the 1- and 3-methyl substituted compounds. The possibility of isolation spiro dienones via photolysis of 6/6-fused cross-conjugated dienones suggested that the conversion of natural products of the α -vetivone type into compounds of the β -vetivone type might be possible.

Isomerization of nootkatone to α -vetivone (also referred to as isonootkatone (12)) has been carried out efficiently by Van der Gen and coworkers (13) with *p*-toluenesulfonic acid in refluxing chloroform. However, in DDQ oxidation of α -vetivone instead of the desired dehydro- α -vetivone 29, a fully conjugated compound 31 was isolated as major product (11). An alternate route of hydrobromination and dehydrobromination was attempted in this research and it provided

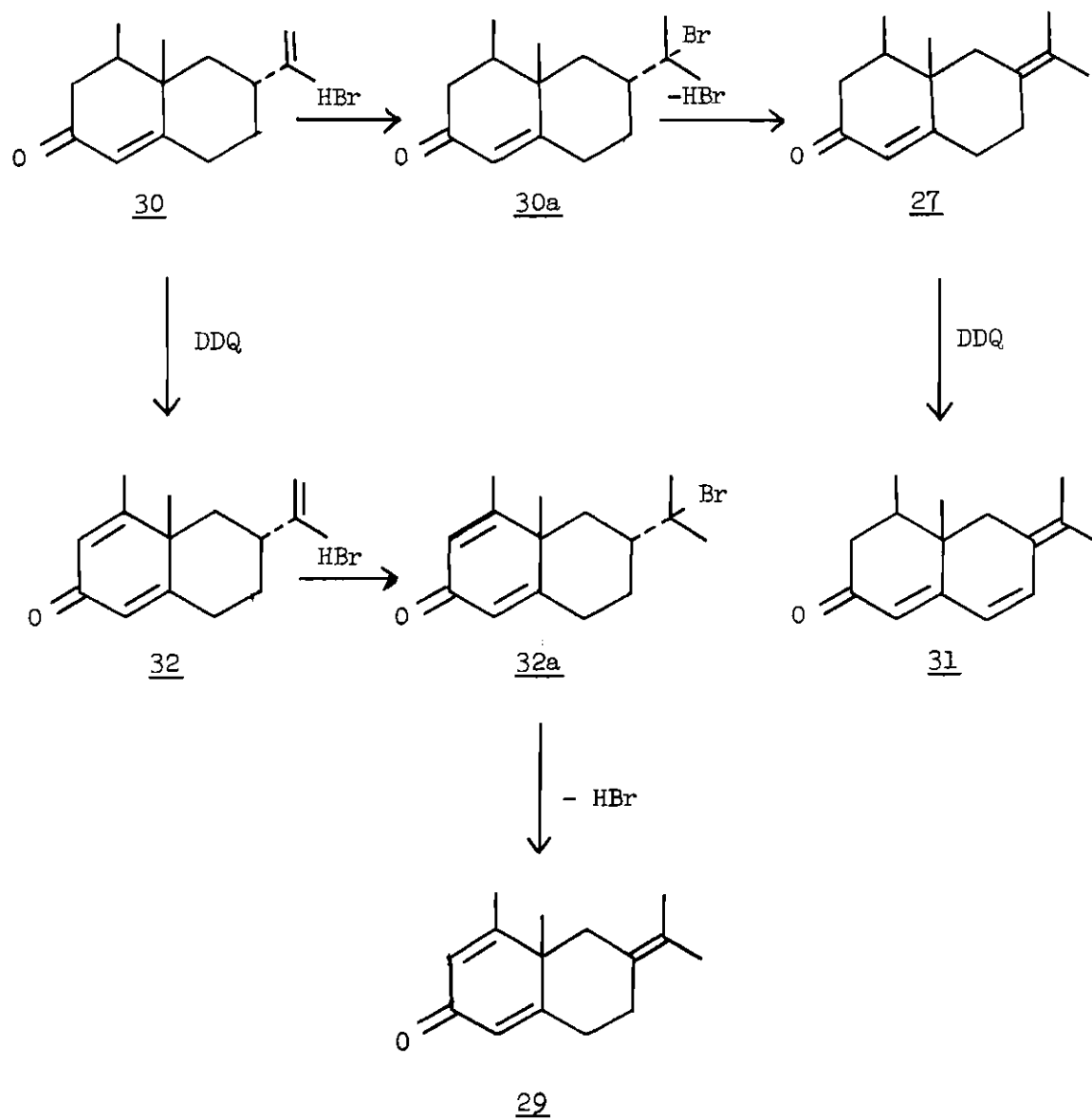


Chart 4. Synthesis of Dehydro- α -vetivone

an adequate solution to the problem of obtaining dehydro- α -vetivone (Chart 4).

Controlled photolyses have been studied in this research to give lumiprodukt 33 and spiro trienone 34. The expected β -vetivone 28 was obtained along with its 10-epimer, 35, via the reduction of spiro trienone 34 (Chart 5).

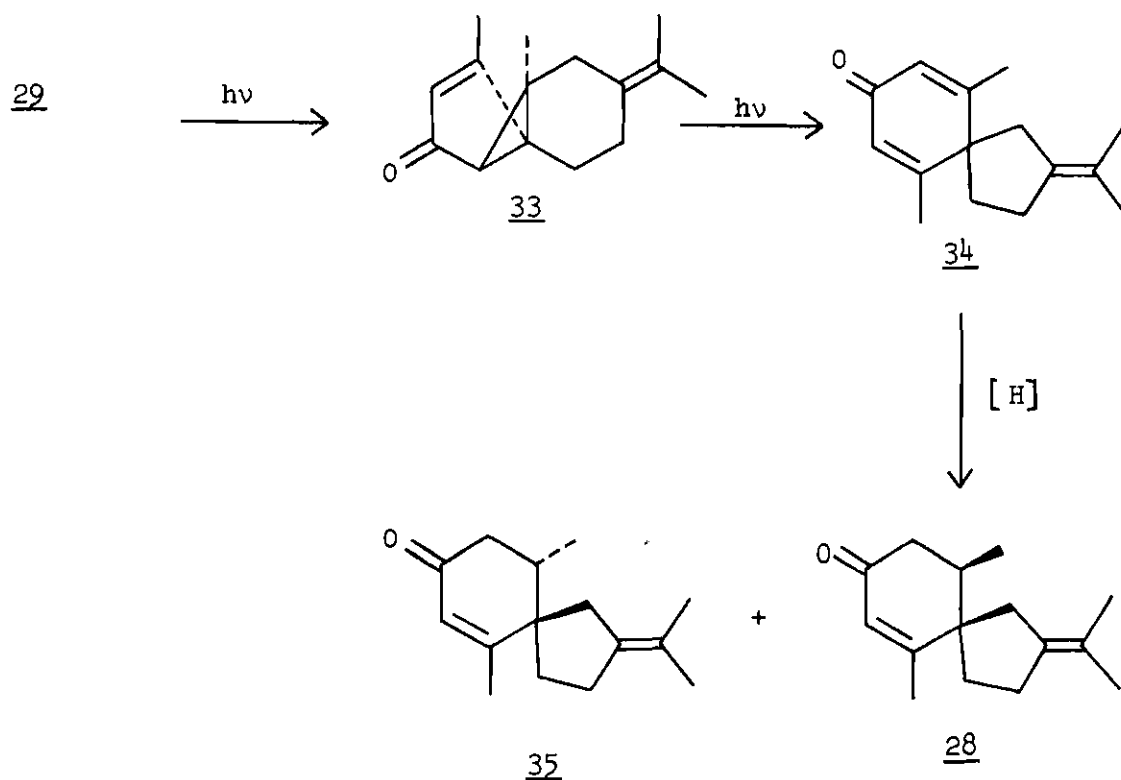


Chart 5. Photolytic Synthesis of 34 and its Reduction

Similar reactions have been done with dehydronootkatone 32 as starting material. In this case three photoproducts were obtained (Chart 6).

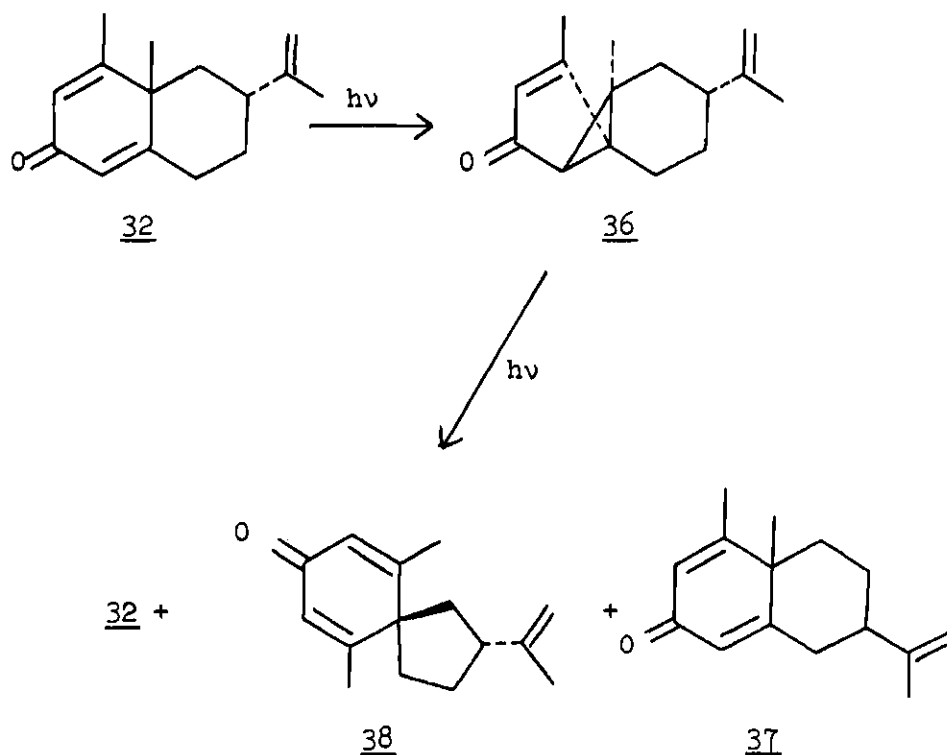
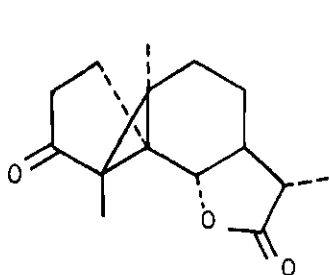
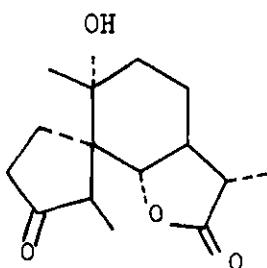
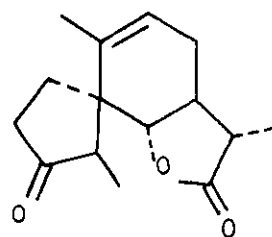
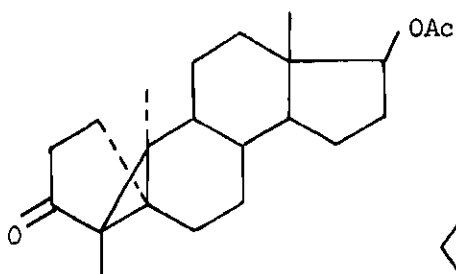
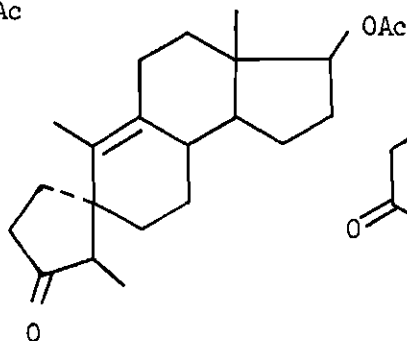
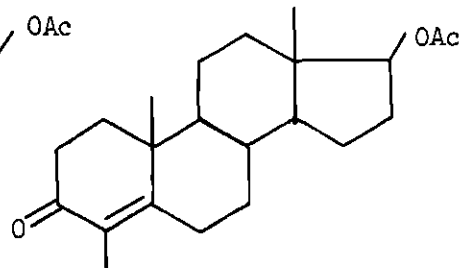
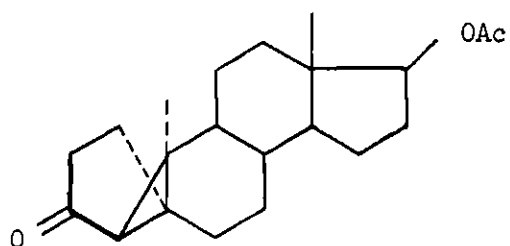
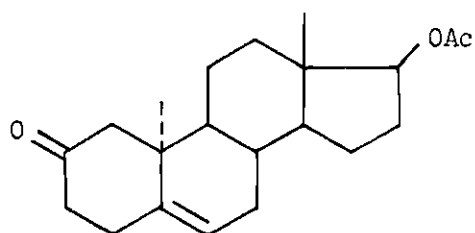


Chart 6. Photolysis of Lumiprodukt 36

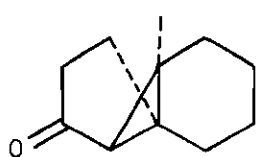
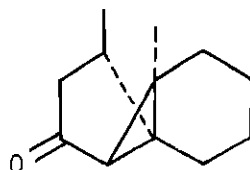
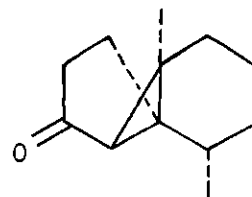
It seemed possible that lumiproduks such as 33 and 36 might be converted into spirocyclic sesquiterpenes by reduction of the conjugated double bond followed by treatment of the conjugated cyclopropyl ketone with acidic reagents. Such a process could lead to opening of the cyclopropane ring to give a tertiary carbonium ion which, by undergoing a 1,2-methylene shift, could yield spirocyclic system.

A few examples of studies of acid promoted opening of the cyclopropane rings of bicyclo[3.1.0]hexan-2-one type compounds have been reported in the literature. It is interesting to see that in these reactions relatively minor structural changes may influence the direction of cleavage of the cyclopropane ring. Lumisantonin 39 was found to undergo cleavage of the 1,4a-bond to give the alcohol 40 and the enone 41 (1). A similar reaction was also observed for the dehydrolumiproduct 42 to give spiro enone 43 and rearranged enone 44 (14). However, dihydrolumitestosterone acetate 45, having no methyl substituent at C-1, was found to give exclusively 46 on treatment with sulfuric acid in acetic acid (15).

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It was also one of the purposes of this research to study some related compounds of this type such as bicyclo[3.1.0]hexan-2-ones 47, 48 and 49. Their behavior under acid treatment should give better understanding of the factors which control the course of the ring opening reaction.

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CHAPTER II

INSTRUMENT AND EQUIPMENT

Infrared spectra were obtained in solution on a Perkin-Elmer Model 457 recording spectrophotometer using 0.1 mm sodium chloride cells. Ultraviolet spectra were obtained on Beckman Model DB-GT recording spectrophotometer using one centimeter matched cells. Nuclear magnetic resonance spectra were obtained on a Varian Associates Model A-60D or T-60A nuclear magnetic resonance spectrometer. Tetramethylsilane was used as an internal standard and the chemical shifts are reported downfield from it. The abbreviations s, d, t, q and m refer respectively to singlet, doublet, triplet, quartet and multiplet; coupling constants J are given in Hz. Melting points were determined on a Fisher Johns hot stage and are uncorrected. Carbon and hydrogen microanalyses were performed by the Atlantic Microlab, Inc., Atlanta, Ga. Mass spectra were obtained on a Hitachi Perkin-Elmer RMU-7 Mass spectrometer. Gas liquid chromatographic analyses were effected using a Perkin-Elmer Model 881 Flame Ionization Gas Chromatograph. Preparative gas liquid chromatography was done using an Aerograph Model A-90D Manual Temperature Programmer Gas Chromatograph.

A Hanovia 450-watt high pressure mercury lamp in a quartz or a Pyrex probe, apparatus similar to that described by Kropp and Erman (16) was used when broad spectrum light source was employed. A Hanau

7-watt low pressure mercury arc lamp which has more than 90 percent of its emission at $2537 \overset{\circ}{\text{\AA}}$ was also used. A slow stream of dried prepurified nitrogen was bubbled through the solution for a 10 minute period prior to and during all irradiations for deoxygenation and agitation of the solution. Solvents were removed under reduced pressure (in vacuo) using a Büchi Rotavapor rotatory evaporator. Hydrogenations were carried out in atmospheric pressure hydrogenation apparatus. Column chromatography was carried out using Grace grade 923, 100 ~ 200 mesh silica gel, 10 percent AgNO_3 impregnated silica gel or Fisher certified grade 80 ~ 200 mesh alumina, Brockman Activity I, acid, neutral or basic. Anhydrous magnesium sulfate was used as drying agent for organic solutions of reaction products in organic solvents unless otherwise specified.

CHAPTER III

EXPERIMENTAL

4,4a,5,6,7,8-Hexahydro-4 α ,4a α -dimethyl-2(3H)-naphthalenone 50

Compound 50 was prepared using the same procedure of Scanio and Starrett (17). Oil dispersed sodium hydride powder (13.0 g, 0.290 moles) was placed under nitrogen in a 1-l round bottom flask equipped with a mechanical stirrer, reflux condenser and dropping funnel. The oil was removed by adding 20 ml of anhydrous hexane to the dispersion and removing the solution formed with a pipet. This operation was repeated three times. Dry nitrogen was passed over the sodium hydride until the solvent was removed and 31.0 g (0.280 moles) of 2-methylcyclohexanone in 600 ml of anhydrous dioxane was added with stirring in a thin stream. The mixture was stirred at reflux for 3 hours and cooled to room temperature. A solution of 23.5 g (0.280 moles) of 3-penten-2-one in 100 ml of anhydrous dioxane was then added dropwise with stirring. The reaction mixture was stirred four days at room temperature and then neutralized with 5 percent hydrochloric acid. After ether extraction and separation, the organic layer was dried and filtered. The solvent was removed in vacuo to yield 42.6 g of crude product as a brown oil. Distillation under reduced pressure gave 25.6 g (52 percent) of a yellow oil (bp 110 ~ 120°/0.2 mm) which according to its nmr spectrum contained 90 percent of 50 and 10 percent of its isomer 51. A small portion of this sample was

chromatographed on silica gel to afford a pure sample of compound 50 (5 percent ether in hexane): uv max (MeOH) 239 nm (ϵ 13,400); ir (CCl_4) 1665 and 1616 cm^{-1} ; nmr (CCl_4) δ 0.94 (d, J = 6 Hz, 3H, C-4 CH_3), 1.05 (s, 3H, C-4a CH_3), 5.63 (br. s, 1H, C-1 H). The nmr spectral properties were identical to that reported (17).

4,4a,5,6,7,8-Hexahydro-4 β ,4 α -dimethyl-2(3H)-naphthalenone (51)

Compound 51 was synthesized in the same way as compound 50 except that DMSO was used as solvent (17). A solution of 31.0 g (0.28 moles) of 2-methylcyclohexanone in 500 ml of DMSO was stirred with 13.0 g (53 percent) (0.29 moles) sodium hydroxide at room temperature for 3 hours under nitrogen. When stirring under nitrogen was continued, a solution of 23.5 g (0.28 moles) of 3-penten-2-one in 100 ml of DMSO was added dropwise. The reaction mixture was stirred for 3 hours at room temperature and then neutralized with 5 percent hydrochloric acid. The reaction mixture was extracted several times with ether and the ether layer was dried over magnesium sulfate. The solvent was removed in vacuo to give a brown oil containing some residual DMSO. Distillation under reduced pressure gave 34.6 g (70 percent) of a yellow oil (bp 110 ~ 120°C/0.2 mm) containing about 95 percent of compound 51 and 5 percent of its isomer compound 50 according to its nmr spectrum. A small portion of this sample was chromatographed on silica gel to afford a pure sample of compound 51 (5 and 10 percent ether in hexane): uv max (MeOH) 239 nm (ϵ 12,100); ir (CCl_4) 1669 and 1617 cm^{-1} ; nmr (CCl_4) δ 0.98 (d, J = 6.5 Hz, 3H, C-4 CH_3), 1.26 (s, 3H, C-4a CH_3), 5.59 (broad s, C-1 H).

5,6,7,8-Tetrahydro-4,4a-dimethyl-2(4aH)-naphthalenone (52)

Compound 52 was prepared using the general procedure of Burn, Kirk and Petrow (18). A solution of 20.0 g (0.11 moles) of 50 and 28.0 g (0.12 moles) of 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) in 500 ml of dry benzene was placed in a 1-l round bottom flask equipped with a mechanical stirrer and a reflux condenser. Glacial acetic acid 3 ml was added and the mixture was stirred at reflux under nitrogen for 48 hours. The mixture was cooled to room temperature, and filtered to remove 2,3-dichloro-5,6-dicyano-p-hydroquinone (DDHQ). The solvent was removed in vacuo and the crude residue was passed through 50 g of neutral alumina column by elution with ether. The solvent was removed in vacuo. Chromatography of the residue on 350 g of basis alumina using hexane-ether as eluent afforded recovery of 4.1 g of enone 50 (5 percent ether in hexane) and 7.8 g (39.4 percent) of dienone 52 (15 and 20 percent ether in hexane). A small portion of the dienone was distilled under reduced pressure to give a colorless oil: bp 114-119°C (bath temperature)/0.2 mm; uv max (MeOH) 245 nm (ϵ 18,400); ir (CCl_4) 1667 (α,β unsaturated C=O) and 1628 cm^{-1} (C=C); nmr (CCl_4) δ 1.28 (s, 3H, C-4aH), 1.94 (d, $J = 0.5$ Hz, 3H, C-4 CH_3), 5.94 (s, 2H, C-1 and C-3 H).

Anal. Calculated for $\text{C}_{12}\text{H}_{16}\text{O}$: C, 81.76; H, 9.16. Found: C, 81.57; H, 9.16.

The same reaction was performed but using enone 51 as starting material. A solution of 24.0 g (0.14 moles) of compound 51 was stirred with 32.0 g (0.14 moles) of DDQ and 10 ml of glacial acetic acid in

500 ml of dry benzene at reflux for 48 hours. The product was worked up and chromatographed on 400 g of basic alumina. Enone 51 (4.6 g) was recovered and 8.2 g (35 percent) of dienone 52 was obtained.

Irradiation of Dienone 52 in Anhydrous Dioxane

A solution of 1.0 g (0.0060 moles) of 52 in 150 ml of anhydrous dioxane was irradiated with a 7-watt low pressure mercury arc lamp for 150 min. The solvent was removed in vacuo and the crude product obtained was chromatographed on 25 g of basic alumina to give 0.62 g (62 percent) of lumipproduct 53 (5 percent ether in hexane) and 0.13 g of starting dienone (15 percent ether in hexane). A small portion of the lumipproduct was distilled under reduced pressure to give a colorless oil: bp 100-105°C (bath temperature)/0.2 mm; uv max (MeOH) 234 nm (ϵ 7,800), 267 nm (ϵ 4,300); ir (CCl_4) 2941, 1695 (α, β unsaturated C=O) and 1671 cm^{-1} (C=C); nmr (CCl_4) δ 1.15 (s, 3H, C-4a angular CH_3), 1.97 (d, $J=1.5$ Hz, 3H, C-4 vinyl CH_3), 5.5 (m, 1H, C-3 vinyl H).

Anal. Calculated for $\text{C}_{12}\text{H}_{16}\text{O}$: C, 81.76; H, 9.16. Found: C, 81.58; H, 9.16.

Irradiation of Lumipproduct 53 in 45 Percent Aqueous Acetic Acid

A solution of 0.5 g lumipproduct 53 in 250 ml of 45 percent aqueous acetic acid was irradiated with a 450-watt high pressure mercury lamp housed in a Pyrex probe. After 29 min. of irradiation the lumipproduct 53 was found to have completely disappeared by glc (19). The solution was extracted well with 80 ml of ether three times. The ether layers were combined and washed several times with brine

water to remove the acetic acid and then dried. Removal of the ether in vacuo afforded 0.43 g of crude product as a brown oil. Chromatography of this oil on 10.0 g of silica gel gave 0.26 g (52 percent) of the spiro dienone 54 (20 percent ether in hexane). Distillation of the product under reduced pressure gave a colorless oil: bp 115-120°C (bath temperature)/0.2 mm; uv max (MeOH) 245 nm (ϵ 12,400); (CCl_4) 1668 (α, β unsaturated C=O) and 1628 cm^{-1} (C=C); nmr (CCl_4) δ 2.01 (s, 6H, two vinyl CH_3), 5.90 (s, 2H, vinyl H).

Anal. Calculated for $\text{C}_{12}\text{H}_{16}\text{O}$: C, 81.76; H, 9.16. Found: C, 81.58; H, 9.23.

3,4-Dehydronootkatone (32)

A solution of 15.0 g (0.069 moles) of 30, 17.0 g (0.075 moles) of DDQ and 5 ml of glacial acetic acid in 400 ml of dry benzene was stirred and heated at reflux for 48 hours under nitrogen. The solution was cooled to room temperature and filtered to remove the DDHQ. The solvent was removed in vacuo and the residue obtained was passed through 50 g of a neutral alumina column by elution with ether. The ether was removed in vacuo. Chromatography of the crude product on 300 g of basic alumina using hexane-ether as eluent afforded 2.4 g (5 percent ether in hexane) of recovered 30 and 5.5 g (37 percent yield) (10, 15 and 20 percent ether in hexane) of a pale yellow oil, identical as compound 32, and having identical physical properties to those previously reported (12): bp 145-150°C (bath temperature)/0.2 mm; uv max (MeOH) 244 nm (ϵ 10,440); ir (CCl_4) 1660 (α, β unsaturated

C=O), 1630 (C=C) and 896 cm^{-1} ; nmr (CCl_4) δ 1.35 (s, 3H, angular CH_3), 1.72 (s, 3H, vinyl CH_3), 1.98 (s, 3H, C-1 vinyl CH_3), 4.73 (s, 2H, $=\text{CH}_2$), and 5.95 (s, 2H, vinyl H).

Anal. Calculated for $\text{C}_{15}\text{H}_{20}\text{O}$: C, 83.28; H, 9.32. Found: C, 83.17; H, 9.42.

Irradiation of 3,4-Dehydronootkatone (32) in Anhydrous Dioxane

A solution of 4.2 g of 32 in 150 ml of anhydrous dioxane was irradiated with a low pressure mercury lamp for 6 hours. Glc analysis (19) of the reaction mixture indicated ca. 85:15 ratio of product and starting material was present at this point. The solvent was removed in vacuo and the crude product obtained was chromatographed on 100 g of basic alumina to give 2.9 g (69 percent) (5 percent ether in hexane) of the lumiprduct 36. Further elution with 15 and 20 percent ether in hexane afforded 0.47 g of recovered dienone 32. Distillation of the photoproduct under reduced pressure gave a colorless oil: bp $129\text{--}134^\circ\text{C}$ (bath temperature)/0.2 mm. A small portion of the oil was further purified by collection on a preparative glc column (22) to obtain an analytical sample: uv max (MeOH) 234 nm (ϵ 3,117), 268 nm (ϵ 1,763); ir (CCl_4) 1682 (α,β unsaturated C=O) 1610 (C=C), and 892 cm^{-1} ; nmr (CCl_4) δ 1.15 (s, 3H, angular CH_3), 1.70 (s, 3H, vinyl CH_3), 2.00 (d, $J=1\text{ Hz}$, 3H, C-4 vinyl CH_3), 4.70 (s, 2H, $=\text{CH}_2$), and 5.52 (broad s, 1H, vinyl H).

Anal. Calculated for $\text{C}_{15}\text{H}_{20}\text{O}$: C, 83.28; H, 9.32. Found: C, 83.22; H, 9.43.

Irradiation of Luminootkatone 36 in 45 Percent Aqueous Acetic Acid

A solution of 2.1 g of 36 in 250 ml of 45 percent aqueous acetic acid was irradiated with 450-watt high-pressure mercury lamp in a Pyrex probe. It was found that no starting material remained after 30 min. of irradiation by glc (19). The photolysis mixture was then extracted with five 50-ml portions of ether. This ether solution was washed several times with brine to remove the acetic acid. Drying over anhydrous sodium sulfate and removal of the solvent in vacuo yielded 2.06 g of crude product as a brown oil. Chromatography of this oil on 50 g of silica gel afforded 0.142 g of 32 (5 percent ether in hexane) which was found to be identical with 3,4-dehydronootkatone by comparison of their uv, ir and nmr spectra. Further elution with 10 percent ether in hexane as eluent gave 0.705 g of a 1:6 mixture of 32 and a second product 37, and further elution with 15 percent ether in hexane gave 0.634 g of a 1:3 mixture of 37 and the third product 38. The fractions eluted by 20 and 30 percent ether in hexane were combined to give 0.472 g of 38: bp 145-150°C (bath temperature)/0.2 mm; uv max (MeOH) 246 nm (ϵ 12,900); ir (CCl_4) 1667 (α, β unsaturated C=O), 1629 (C=C), and 892 cm^{-1} ; nmr (CCl_4) δ 1.79 (s, 3H, vinyl CH_3), 2.06 (s, 6H, two vinyl CH_3 on ring), 4.76 (d, $J = 1$ Hz, 2H, $=\text{CH}_2$) and 5.87 (s, 2H, two vinyl H on ring). The exact mass was calculated for $\text{C}_{15}\text{H}_{20}\text{O}$ as 216.1514 and found as 216.1524. The nmr and ir spectra of this compound were identical to the spectra of anhydro- β -rotunol kindly supplied by Dr. Hikino (20b).

Anal. Calculated for $\text{C}_{15}\text{H}_{20}\text{O}$: C, 83.28; H, 9.32. Found: C,

83.20; H, 9.40.

Repeated column chromatography on 50 g of silica gel of the mixtures afforded totally 0.252 g (12 percent) of 32, 0.943 g (45 percent) of 38 and 0.758 g (36 percent) of 37 which was found as a pale yellow oil: bp 143-150°C (bath temperature)/0.2 mm. A small portion of this oil was further purified by collection on a preparative glc column (22) to give an analytical sample: uv max (MeOH) 245 nm (ϵ 19,100); ir (CCl_4) 1668 (α, β unsaturated C=O), 1631 (C=C) and 898 cm^{-1} ; nmr (CCl_4) δ 1.32 (s, 3H, angular CH_3), 1.78 (s, 3H, vinyl CH_3), 1.99 (s, 3H, C-4 vinyl CH_3), 4.78 (s, 2H, $=\text{CH}_2$) and 5.97 (s, 2H, C-1 and C-3 vinyl H). The exact mass was calculated for $\text{C}_{15}\text{H}_{20}\text{O}$ as 216.1514 and found as 216.1524.

Anal. Calculated for $\text{C}_{15}\text{H}_{20}\text{O}$: C, 83.28; H, 9.32. Found: C, 83.20; H, 9.40.

Dihydrocarvone (55)

A solution of 50.0 g (0.34 moles) of 1-carvone, 125 g (1.9 moles) of zinc dust and 62.5 g (1.6 moles) of sodium hydroxide in 375 ml of water and 650 ml of 95 percent ethanol was stirred and heated at reflux for 5 hours with stirring under nitrogen. The stirrer was removed and 650 ml of ethanol was removed by distillation. The residual solution was then steam distilled until ca. 2 l of distillate was collected. The distillate was extracted with ether and dried. The solvent was removed in vacuo to afford 25.0 g of oil which was found to be a mixture of trans and cis 55 by glc (19); bp 55 ~ 60°C/0.2 mm.

Reaction of Dihydrocarvone (55) with 3-Penten-2-one

The procedure of Leitereg (21) was followed. A solution of 24.0 g (0.16 moles) of dihydrocarvone 55 and 7.2 g (0.16 moles) of 53 percent sodium hydride in mineral oil in 250 ml of dry dioxane was refluxed 1.5 hours with stirring under nitrogen. The reaction mixture was cooled to room temperature and a solution of 13.2 g (0.16 moles) of 3-penten-2-one in 50 ml of dioxane was added dropwise with stirring over a period of 1.5 hours. After 24 hours of continued stirring, the reaction mixture was neutralized with 5 percent hydrochloric acid and then extracted with three 200 ml portions of ether. The organic layers were combined and dried. The solvent was removed in vacuo and the residue obtained was distilled under reduced pressure to give 15.0 g of dihydrocarvone (bp 30-60°C/0.2 mm) and 13.0 g (38 percent) of octalone product (60-117°C/0.2 mm). This product was found to be mixture of enones of type 56 by glc and nmr analysis. This mixture was oxidized with DDQ without further purification.

Oxidation of Enone 56 with DDQ

A solution of 5.0 g (0.023 moles) of 56 and 6.1 g (0.027 moles) of DDQ in 100 ml of dry benzene containing 1 ml of glacial acetic acid was refluxed 48 hours with stirring under nitrogen. The solution was cooled to room temperature, filtered and passed through 35 g of neutral alumina by elution with ether. The solvent was removed in vacuo. The residue was chromatographed on 120 g of basic alumina to yield 1.2 g of starting enone (hexane and 5 percent ether in hexane) and 1.7 g

(34 percent yield, 10 and 15 percent hexane) of oily product which was found to be a mixture of the cis and trans isomer of 57 in a ratio of 3:7 by glc (19). Preparative glc separation (22) of this product gave a sample which contained greater than 85 percent cis isomer. The spectral properties of this sample were identical to those of 37 by comparison of their ir, uv and nmr spectra.

Irradiation of Trienone 32 in 45 Percent Aqueous Acetic Acid

A solution of 0.10 g of trienone 32 in 2.5 ml of 45 percent aqueous acetic acid was placed in a uv cell and irradiated for 450 min. with the high pressure lamp housed in a Pyrex probe. The transparent side of uv cell was attached on the Pyrex probe. The solution was agitated and deoxygenated by passing nitrogen through a needle projecting to the bottom of the uv cell. After the irradiation the solution was extracted with 10 ml of ether. The ether solution was washed with brine water to remove acetic acid and then dried. Removal of the solvent in vacuo yielded 89 mg of a brown oil which was found by glc (19) to be a mixture of 32, 37, and 38 in a ratio of ca. 2:1:1.

Irradiation of Trienone 37 in 45 Percent Aqueous Acetic Acid

A solution of 0.15 g of trienone 37 in 2.5 ml of 45 percent aqueous acetic acid was irradiated for a 60 min. period the same way as described for 32. During the irradiation the composition of the reaction mixture was monitored by glc (19). After 15 min. of irradiation, peaks corresponding to 32, 37 and 38 were as before found in a 1:10:2 ratio. After 60 min., the same work up as before

gave 0.12 g of a brown oil which was found to be a mixture of 32, 37 and 38 in a ratio fo ca. 1:3:2 by glc (19).

Irradiation of Trienone 38 in 45 Percent Aqueous Acetic Acid

A solution of 0.15 g of trienone 38 in 2.5 ml of 45 percent aqueous acetic acid was irradiated for a 60 min. period the same way as described for 32 and 37. During the irradiation the composition of the reaction mixture was monitored by glc (19). After 15 min. of irradiation, peaks corresponding to 32, 37 and 38 were found in a 2:3:8 ratio. After 60 min., the same work up as before gave 0.13 g of a brown oil which was found to be a mixture of 32, 37 and 38 in a ratio of ca. 2:3:2 by glc (19).

Irradiation of Trienone 37

A solution of 0.15 g of trienone 37 in 100 ml of anhydrous dioxane was irradiated with a low pressure mercury lamp for 6 hours. The solvent was removed in vacuo to give a yellow oil which on glc (19) exhibited a peak of similar retention time to that of 36. Without purification this oil was further irradiated with high pressure mercury lamp in 45 percent aqueous acetic acid for a total of 30 min. in the same way as described for 36. During the irradiation, the composition of the reaction mixture was monitored by glc (19). After 5 min. of irradiation, it was found that two new peaks were present in a ratio of 15:85. After 30 min. of irradiation the same work up as described before gave a brown oil which according to glc analysis (19) was a mixture of 32, 37 and 38 in a ratio of 2:2:3.

Irradiation of Trienone 38

A solution of 0.10 g of trienone 38 in 100 ml of anhydrous dioxane was irradiated with a low pressure mercury lamp for 6 hours to give a yellow oil which on glc (19) exhibited a mixture of four peaks close together of similar retention time to that of 36. Without purification this oil was further irradiated with a high pressure mercury lamp in 45 percent aqueous acetic acid and monitored in the same way as described for 37. After 5 min. of irradiation, it was found that two peaks were produced in a ratio of 1:1. After 30 min. of irradiation the same work up as described before gave a brown oil which according to glc analysis (19) was a mixture of 32, 37 and 38 in a ratio of 2:3:2.

Attempted Irradiation of Trienone 32 in 45 Percent Aqueous

Acetic Acid with Quartz Probe

A solution of 0.2 g trienone 32 in 2.5 ml of 45 percent aqueous acetic acid was irradiated for a period of 2 hours the same way as before except a quartz probe was employed. The same work up gave 0.15 g of a brown oil which was found to be a mixture of two groups of compounds by glc (19). The first group was a mixture of 32, 37 and 38 which consisted ca. 25 percent of the total volatile products. The second group with longer retention time was made up mainly of two broad peaks which consisted ca. 75 percent of the products. Attempts at separation and purification of these products were unsuccessful.

α -Vetivone (27)

Compound 27 was prepared by isomerization of nootkatone (30)

in similar way to that described by Van der Gen and coworkers (13). A solution of 2.0 g of nootkatone (30) and 0.4 g of *p*-toluenesulfonic acid in 22.0 ml of chloroform was refluxed with stirring for 65 hours. After it had been cooled to room temperature, the dark solution was neutralized with 5 percent of aqueous sodium bicarbonate. The organic layer was separated and dried. The solvent was removed in vacuo and the residue was distilled under reduced pressure to yield 1.82 g of pale yellow oil, bp 100 - 110°C/0.2 mm. This oil was found to be a mixture of 27 and 30 in 7:1 ratio by glc (19). Chromatography on 50 g of 10 percent silver nitrate impregnated silica gel gave 0.23 g of recovered 30 and 1.49 g (75 percent) of 27. Distillation of 27 under reduced pressure gave a colorless oil: bp 125-130°C (bath temperature)/0.2 mm; uv max (MeOH) 239 nm (ϵ 14,000); ir (CCl_4) 1671 (α,β unsaturated C=O) and 1621 cm^{-1} (conj. C=C); nmr (CCl_4) δ 0.97 (s, 3H, angular CH_3), 1.01 (d, $J = 6$ Hz, 3H, C-1 CH_3), 1.75 (s, 6H, $=\text{C}(\text{CH}_3)_2$), 5.69 (s, 1H, vinyl H).

The method of hydrobromination and then dehydrobromination was also found to be successful in the conversion of nootkatone (30) to α -vetivone (27). Nootkatone (30) (1.32 g) in 40.0 ml of glacial acetic acid was cooled in an ice bath with stirring. Hydrogen bromide in acetic acid (32 percent) (4.5 ml) was added slowly. The mixture was allowed to stir for 90 min. at 10°C and then 10 min. at room temperature. After addition of 100 ml of ether, the reaction mixture was neutralized with 5 percent sodium bicarbonate. The organic layer was separated and dried over anhydrous magnesium sulfate. The solvent was removed in vacuo to yield 1.8 g of a brown oil. The nmr spectrum of the crude

product showed that addition of hydrogen bromide to the side chain had occurred. The bromo enone structure 30a was assigned on the basis of its nmr spectrum: (CCl_4) δ 0.98 (d, $J = 4$ Hz, 3H, C-1 CH_3), 1.11 (s, 3H, angular CH_3), 1.81 (br. s, 6H, $-(\text{CH}_3)_2\text{Br}$), 5.69 (s, 1H, vinyl H).

A solution of the crude bromo enone (1.65 g, 0.0055 moles) in 50.0 ml acetone containing 2.2 g (0.0078 moles) of 2,6-lutidine was stirred under nitrogen for 2 hours at 50°C (23). The solvent was removed in vacuo, 100 ml of a mixture of 1:1 ether-water was added to the reaction mixture, and the ether layer was separated and dried. The residue was distilled under reduced pressure to give 0.87 g of a pale yellow oil (bp $120\text{--}135^\circ\text{C}$ (bath temperature)/0.2 mm) which was found to be composed of a mixture of 27 and 30 in a ratio of 8:1 by glc (19). Chromatography of this oil on 20 g of 10 percent silver nitrate impregnated silica gel gave 0.084 g of recovered 30 and 0.670 g (82 percent) of α -vetivone as a colorless oil.

3,4-Dehydro- α -vetivone (29)

A solution of 4.0 g of dienone 32 in 50 ml of glacial acid was cooled to 10°C and stirred while 10 ml of 32 percent hydrogen bromide in acetic acid was added slowly. The mixture was allowed to stir for 90 min. at 10°C and then 10 min. at room temperature. After addition of 100 ml of ether, the reaction mixture was neutralized with 5 percent aqueous sodium bicarbonate. The organic layer was separated and the aqueous solution was extracted with another 100-ml portion of ether. The solution was dried and filtered. The solvent was removed in vacuo to yield 5.25 g of a brown oil. A small portion of this crude product

was examined by spectroscopic methods and the structure 32a was assigned according to its spectral properties: uv max (MeOH) 240 nm (ϵ 19,000); ir (CCl_4) 1664 (α, β unsaturated C=O) and 1629 cm^{-1} ; nmr (CCl_4) δ 1.32 (s, 3H, angular CH_3), 1.75, 1.78 (2s, 6H, $-(\text{CH}_3)_2\text{Br}$), 2.01 (s, 3H, vinyl CH_3), 5.94 (s, 2H, vinyl H).

The crude bromo dienone 5.0 g (0.017 moles) was dissolved in 50 ml of acetone and stirred with 8.1 g (0.0251 moles) of tetra-n-butyl-ammonium bromide and 1.93 g (0.0181 moles) of 2,6-lutidine under nitrogen for 2 hours at 50°C (23). The solvent was removed in vacuo and a 1:1 ether-water mixture (100 ml) was added. The ether layer was separated and the aqueous layer was extracted by another 50-ml portion of ether. The solution was dried and the solvent was removed in vacuo. The residue obtained was a brown oil. Analysis of the residual oil by nmr and glc indicated that it was composed of 29 and 32 in an 8:1 ratio. Chromatography of the oil on 100 g of 10 percent silver nitrate impregnated silica gel gave 0.37 g of recovered 32 and 3.08 g (85 percent) of 29. Distillation of the latter gave a colorless oil which solidified on standing. Recrystallization from hexane afforded a long white prisms: mp 79-80°C, uv max (MeOH) 239 (ϵ 16,200) and 263 nm (ϵ 12,700); ir (CCl_4) 1663 (α, β unsaturated C=O) and 1630 cm^{-1} (conj. C=C) nmr (CCl_4) δ 1.16 (s, 3H, angular CH_3), 1.77 (br. s, 6H, $=(\text{CH}_3)_2$), 2.01 (s, 3H, vinyl CH_3), 5.93 (s, 2H, vinyl H).

Anal. Calculated for $\text{C}_{15}\text{H}_{20}\text{O}$: C, 83.28; H, 9.32. Found: C, 83.36; H, 9.40.

Irradiation of Trienone 29 in Anhydrous Dioxane

A solution of 1.26 g (0.0058 moles) of trienone 29 in 125 ml of anhydrous dioxane was irradiated for 5 hours with a low-pressure mercury lamp. After removing the solvent in vacuo the residue was chromatographed on 40 g of basic alumina. Elution with hexane and 5 percent ether in hexane gave 0.75 g (61 percent) of lumi- α -vetivone (33) and elution with 10, 15 and 20 percent ether in hexane gave 0.24 g of recovered dienone 29. Distillation of 33 gave a colorless oil: bp 129-134°C (bath temperature)/0.2 mm; uv max (MeOH) 232 ($\epsilon = 6,110$) and 267 nm (ϵ 3,300); ir (CCl_4) 1685 (α, β unsaturated C=O) and 1609 cm^{-1} (conj. C=C), nmr (CCl_4) δ 1.16 (s, 3H, angular CH_3), 1.65 (br. s, 6H, $=\text{C}(\text{CH}_3)_2$), 1.98 (s, 3H, vinyl CH_3), and 5.47 (s, 1H, vinyl H).

Anal. Calculated for $\text{C}_{15}\text{H}_{20}\text{O}$: C, 83.28; H, 9.32. Found: C, 83.37; H, 9.32.

Irradiation of Lumi- α -vetivone (33)

in 45 Percent Aqueous Acetic Acid

A solution of 0.39 g (0.0018 moles) of ketone 33 in 300 ml of 45 percent aqueous acetic acid was irradiated 15 min. with a high-pressure mercury lamp. The acetic acid solution was extracted thoroughly with 300 ml of ether. The ether layer was washed with 5 percent sodium bicarbonate solution until the acetic acid was neutralized. The organic layer was separated and dried. After the ether was removed in vacuo, the residue obtained was chromatographed on a 10 g of neutral alumina to yield 0.195 g of a pale yellow oil (10, 15 and 20 percent ether in hexane). Distillation of this oil under reduced pressure gave

a colorless oil which solidified on standing. Recrystallization from hexane afforded a white crystals of 34: mp 76-78°C; uv max (MeOH) 244 nm (ϵ 6,400); nmr (CCl_4) δ 1.68 (br. s, 6H, $=\text{C}(\text{CH}_3)_2$), 1.92 (s, 6H, two vinyl CH_3 's), 5.80 (s, 2H, two vinyl H's).

Anal. Calculated for $\text{C}_{15}\text{H}_{20}\text{O}$: C, 83.28; H, 9.32. Found: C, 83.08; H, 9.36.

Irradiation of Dehydro- β -vetivone (34)

A solution of 94 mg (0.44 moles) of 34 in 2.5 ml of anhydrous dioxane was placed in an uv cell and irradiated with a low pressure mercury lamp for 110 min. Removal of the solvent yielded 87 mg of a brown oil which was found to give four peaks in glc analysis (19). The first with shortest retention time amounted 20 percent of the product and was not identified. The second and third were not well resolved and consisted 40 percent of the product. The fourth peak corresponded to that of unreacted starting material. The second and third peaks were collected by preparative glc (22) and from 68 mg of crude residue 21 mg of colorless oil was obtained. The structures 58a and 58b were assigned as this mixture on the basis of spectral properties: uv max (MeOH) 227 nm (ϵ 12,700), 266 nm (ϵ 6,300); ir (CCl_4) 1689 (α,β unsaturated $\text{C}=\text{O}$) and 1662 cm^{-1} ; nmr (CCl_4) δ 1.40 (s, 3H, angular CH_3), 1.60 (br. s, 6H, $=\text{C}(\text{CH}_3)_2$), 1.97 (d, $J = 1.5$ Hz, 3H, vinylar CH_3), 5.40 (br. s, 1H, vinyl H).

Irradiation of this sample (50 mg in 2.5 ml of 45 percent aqueous acetic acid) was performed in an uv cell with a high pressure mercury lamp and Pyrex probe. After a 20-min. period of irradiation the

reaction mixture was worked up as before to give 50 mg of brown oil which was found to be identical with dienone 29 by a comparison of their nmr spectra.

Hydrogenation of Dehydro- β -vetivone (34)

A solution of 50 mg (0.23 mmoles) of dienone 34 in 0.5 ml of anhydrous ethanol was injected into a reaction mixture which was prepared by stirring 5 mg of 5 percent palladium on calcium carbonate in 5 ml of anhydrous ethanol for 2 hours under hydrogen at atmospheric pressure. The absorption of hydrogen was observed immediately and interrupted after 1 equivalent (~ 5.7 ml) of hydrogen was taken up. After removal of the catalyst by filtration and removal of the solvent in vacuo, the crude product was found to be a mixture of tetrahydro derivatives of 34, dihydro derivatives of 34 and unreacted dienone in a ratio of ca. 2:3:2 according to its glc analysis (19). Preparative glc collection (22) of this crude product yielded 11.5 mg of a colorless oil which appeared to be a mixture of saturated ketones 59 (nmr spectrum showed no vinyl hydrogen present) followed by 17.5 mg of a colorless oil which was a mixture of β -vetivone (28) and its 10-epimer 35 in a ratio of ca. 7:3. The ratio of 28 and 35 was determined by comparison of this mixture with an authentic sample of β -vetivone isolated from vetiver oil (24). However, the spectral properties of 35 including its uv, ir and nmr (60 Mc) spectra were found similar to that of 28. It was reported by McCurry (38) that different nmr was found on a 250 Mc nmr machine. The glc (19) retention times were measured as 14.6 min. for 28 and 15.5 min. for 35

at 200°C (isothermal) and were also reported by McCurry (38) as 22.6 min. for 28 and 23.6 min. for 35 at 220°C and on a 10 foot column of 20 percent Craig on 60/80 Chromosorb W.

Isolation of α - and β -Vetivone from Vetiver Oil

The method of Dawson (24) was used for this isolation. A solution of 50.0 g oil of vetiver, 10.0 g of Girard's T reagent, and 15 ml of glacial acetic acid in 200 ml of 95 percent alcohol was heated at reflux for 2 hours. Following removal of 175 ml of the alcohol by distillation, 100 ml of water was added. The remaining aqueous solution was acidified with 10 ml of concentrated hydrochloric acid and heated for 20 min. on steam bath. After being allowed to cool to room temperature the reaction mixture was extracted thoroughly with ether and then dried. The solvent was removed in vacuo to give a yellow oil. The oil was distilled and the fraction boiling at 100-130°C was subjected to preparative glc (22) at 205°C. The retention time of β -vetivone was 65 min. while that of α -vetivone was 72 min. The following spectral data were observed. For α -vetivone 27: nmr (CCl_4) 0.97 (s, 3H, angular CH_3), 1.01 (d, $J = 6$ Hz, 3H, $-\text{CH}-\text{CH}_3$) 1.75 (br. s, 6H $=\text{C}(\text{CH}_3)_2$), and 5.69 (br. s, 1H, vinyl H). For β -vetivone 28: nmr (CCl_4) δ 0.91 d, $J = 6.5$ Hz, 3H, $-\text{CH}-\text{CH}_3$), 1.61 and 1.67 (s, 3H, $=\text{C}(\text{CH}_3)_2$), 1.84 (d, $J = 1$ Hz, 3H, vinyl CH_3) and 5.65 (br. s, 1H, vinyl H).

Lithium Ammonia Reduction of Dehydro- β -vetivone (34)

In a 50 ml three-necked flask equipped with a glass magnetic stirrer and a dry ice-acetone condenser was flame-dried and 30 ml of anhydrous ammonia (distilled from sodium) was introduced under nitrogen.

To this was added 8.0 mg (1.2 mmoles) of freshly cut lithium wire, followed by a solution of 123 mg (0.570 mmoles) of 34 and 42.2 mg (0.570 mmoles) of dry tert-butyl alcohol in 5 ml of ether using a syringe. The reaction mixture was stirred under this dry ice cooled temperature for 35 min. and then was treated with 0.5 g of ammonium chloride. Removal of the dry ice-acetone condenser and the ammonia was allowed to evaporate at room temperature. A mixture of 20 ml of ether and 30 ml of water was added. After separation, the aqueous layer was extracted with 30 ml of ether and the ether layers were combined and dried. The ether was removed in vacuo to yield 112 mg of crude material. Distillation of this crude product under reduced pressure to give a colorless oil (bp 130-135°C (bath temperature/0.2 mm)) which was found to be a mixture of β -vetivone (28) and its 10-epimer 35 in a ratio of 3:7 by glc (19).

Hydrogenation of Dehydro- α -vetivone (29)

A solution of 50.0 mg (0.231 mmoles) of dienone 29 in 0.5 ml of anhydrous ethanol was injected into a reaction mixture which was prepared by stirring 5 mg of palladium on carbon in 5 ml of anhydrous ethanol for 2 hours under a hydrogen atmosphere. After one equivalent (~ 5.7 ml) of hydrogen was absorbed, the reaction was stopped, and the reaction mixture was filtered to remove the catalyst. The solvent was removed and the residue obtained was found to be a mixture of at least four compounds by glc (19). None of them corresponded to the desired α -vetivone by comparing their retention times with that of the natural product. Further identification of these products were not successful.

Other catalysts such as 5 percent palladium on calcium carbonate and the homogeneous catalyst tris(triphenylphosphinyl)-rhodium chloride were tried, but no reduction occurred under the conditions employed.

Lithium-Ammonia Reduction of Dehydro- α -vetivone (29)

In a 50 ml three-necked flask equipped with a glass magnetic stirrer and a dry ice-acetone condenser was flame dried, and 30 ml of anhydrous ammonia (distilled over sodium) was introduced under nitrogen. To this was added 6.8 mg (0.98 mmoles) of freshly cut lithium wire, followed by a solution of 100 mg (0.453 mmoles) of 29 and 34.3 mg (0.463 mmoles) of dry tert-butyl alcohol in 5 ml of ether using a syringe. This reaction mixture was stirred at the reflux temperature of liquid ammonia (ca. - 33°C) for 30 min. and then was treated with 0.5 g of ammonium chloride. Following removal of the dry ice-acetone condenser and the ammonia was allowed to evaporate at room temperature. A mixture of 20 ml of ether and 30 ml of water was added. After separation, the aqueous layer was extracted with 30 ml of ether and the ether layers were combined and dried. The ether was removed in vacuo to yield 99 mg of crude material as a brown oil. Hickman microdistillation of this oil under reduced pressure gave 81 mg of colorless oil 60: bp 130-140°C (bath temperature)/0.2 mm; ir max (CCl₄) 3610 (free -OH), 3600-3100 (-OH hydrogen bonded), 1610, 1595, 1485 and 1456 cm⁻¹ (aromatic); nmr (CCl₄) δ 1.62 (br. s, 9H, three vinyl CH₃), 2.08 (s, 3H, aromatic CH₃), 2.16 (s, 3H, aromatic CH₃), 6.42 (s, 2H, aromatic H).

Irradiation of Dienone 61 in Anhydrous Dioxane

A solution of 0.8 g of dienone 61 in 150 ml of anhydrous dioxane was irradiated for 2.5 hours with low pressure mercury lamp. The solvent was removed in vacuo and the crude product was distilled under reduced pressure to give 0.65 g of a colorless oil which according to its physical properties was found to be identical with those reported for the lumiprodukt 62 (25). uv max (MeOH) 236 nm (ϵ 6,100); ir (CCl_4) 1697 cm^{-1} (α, β unsaturated C=O), nmr (CCl_4) δ 1.18 (s, 3H, angular CH_3), 5.79 (d, $J = 5$ Hz, 1H, C-2 vinyl H), 7.15 (d, $J = 5$ Hz, 1H, C-1 vinyl H).

Irradiation of Lumiprodukt 62 in

45 Percent Aqueous Acetic Acid

A solution of 100 mg of lumiprodukt 62 in 2.5 ml of 45 percent aqueous acetic acid was irradiated in the usual way with a high pressure mercury lamp in a Pyrex probe for 40 min. The same work up as in irradiation of compound 53 afforded 96 mg of crude product. Distillation of this material under reduced pressure gave 62 mg of 63 as a colorless oil: bp 80-85°C (bath temperature)/0.2 mm; uv max (MeOH) 238 nm (ϵ 16,300) and 243 nm (ϵ 15,700); ir (CCl_4) 1667 (α, β unsaturated C=O) and 1629 cm^{-1} (conj. C=C); nmr (CCl_4) 1.93 (d, $J = 1$ Hz, 3H, vinyl CH_3) 5.98 (d, $J = 10$ Hz, 1H), 5.99 (s, 1H), 6.91 (d, $J = 10$ Hz, 1H).

Anal. Calculated for $\text{C}_{11}\text{H}_{14}\text{O}$: C, 81.43; H, 8.70. Found: C, 81.22; H, 8.80.

Irradiation of Lumiprodukt 62 in 45 Percent

Aqueous Acetic Acid with Quartz Filter

A solution of 50 mg of lumiprodukt 62 in 2.5 ml of 45 percent aqueous acetic acid was irradiated in the same way except a quartz probe was used. After 30 min., the crude product was worked up as usual. Distillation under reduced pressure afforded 31 mg of a colorless oil which solidified on standing. Recrystallization twice from hexane gave a white crystals which were found to have identical properties to those reported (26) for the phenol 64: mp 102-103°C; ir max (CCl₄) 3610 (-OH), 3600-3616 broad (H-bonding), 2935, 2860 (C-H stretching), 1614, 1599, 1480 and 1462 cm⁻¹ (aromatic). nmr (CCl₄) δ 2.09 (s, 3H, aromatic CH₃), 4.30 (br. s, 1H, -OH), 6.30, 6.35 (two br. s, aromatic H).

Thermal Isomerization of the Spiro dienone 63

in 45 Percent Aqueous Acetic Acid

A solution of 15 mg of dienone 63 in 5 ml of 45 percent aqueous acetic acid was refluxed 2 hours with stirring. The reaction mixture was extracted with 10 ml of ether which was washed with 2 percent sodium bicarbonate until the acetic acid was removed and then dried. The solvent was removed in vacuo to give 13.8 mg of crude product. This material was found to be identical with the phenol 64 obtained as described above.

Hydrogenation of Lumiprodukt 53

A solution of 230 mg (1.29 mmoles) of lumiprodukt 53 in 1 ml of anhydrous ethanol was injected into a reaction mixture prepared

by stirring 25 mg of 5 percent palladium on carbon in 3 ml of anhydrous ethanol for 2 hours under a hydrogen atmosphere at room temperature. After 3 hours, one equivalent (29 ml) of hydrogen was absorbed. The reaction mixture was filtered and the solvent was removed in vacuo. The crude product was distilled under reduced pressure to give 217 mg of colorless oil 48: bp 92-96°C (bath temperature)/0.2 mm; ir max (CCl₄) 1719 cm⁻¹ (conj. cyclopropyl C=O); nmr (CCl₄); δ 1.28 (s, 3H, angular CH₃), 1.14 (d, J = 6.5 Hz, 3H, C-1 CH₃).

Anal. Calculated for C₁₂H₁₈O: C, 80.84; H, 10.18. Found: C, 80.94; H, 10.17.

Hydrogenation of Lumiprodukt 62

A solution of 189 mg (1.15 mmoles) of lumiprodukt 62 in 5 ml of anhydrous ethanol with 5 ml of anhydrous ethanol was hydrogenated over 30 mg of 5 percent palladium in the same way as described for compound 53. The crude product obtained was distilled under reduced pressure to give 175 mg of colorless oil 47: bp 90-95°C (bath temperature)/0.2 mm; ir max (CCl₄) 1720 cm⁻¹ (conj. cyclopropyl C=O); nmr (CCl₄) δ 1.14 (s, 3H, angular CH₃).

Anal. Calculated for C₁₁H₁₆O: C, 80.43; H, 9.83. Found: C, 80.42; H, 9.84.

Irradiation of Dienone 65 in Anhydrous Dioxane

A solution of 1.20 g (0.0068 moles) of dienone 65 in 150 ml of anhydrous dioxane was irradiated with a low pressure mercury lamp for 3.5 hours. The solvent was removed in vacuo and the residue was distilled under reduced pressure to afford 1.09 g (91 percent) of 66

as a colorless oil: bp 95-100°C (bath temperature)/0.2 mm; uv max (MeOH) 236 mm (ϵ 5,600); ir (CCl_4) 1690 (α, β unsaturated C=O) and 1602 cm^{-1} (conj. C=C); nmr (CCl_4) δ 1.18 (s, 3H, angular CH_3), 5.78 (AB quartet, J_{AB} = 5.5 Hz, 1H, C-3H), 7.38 (AB quartet, J_{AB} = 5.5 Hz, 1H, C-4 H).

Hydrogenation of Lumiprduct 66

A solution of 796 mg of lumiprduct 66 in 15 ml of anhydrous ethanol was hydrogenated over 80 mg of 5 percent palladium on carbon in the same way as was described for compound 53. The crude product was distilled under reduced pressure to give 760 mg (95 percent) of 49 as a colorless oil: bp 95-100°C (bath temperature)/0.2 mm; ir (CCl_4) 1722 cm^{-1} (conj. cyclopropyl C=O); nmr (CCl_4) δ 1.06 (d, J = 7 Hz, 3H, -CH- CH_3), 1.14 (s, 3H, angular CH_3).

Reaction of the Dihydrolumiprduct 48 with

Hydrogen Bromide Followed by Dehydrobromination

To a solution of 150 mg (0.843 mmoles) of dihydrolumiprduct 48 in 5 ml of glacial acetic acid was added 0.5 ml of a 32 percent hydrogen bromide in acetic acid dropwise with stirring at room temperature. The reaction mixture was stirred for 5 min. then extracted with 10 ml of ether. The aqueous layer was further extracted with two 15-ml portions of ether. The ether layers were combined and washed with 5 percent sodium bicarbonate to remove the acetic acid. The solution was dried, filtered, and the solvent removed in vacuo. The crude product was a brown oil and was assigned the bromo ketone

structure 67 on the basis of its nmr spectrum: (CCl_4) δ 1.31 (d, $J = 7$ Hz, 3H, $-\text{CH}-\text{CH}_3$) and 1.89 (s, 3H, $-\text{CBr}-\text{CH}_3$). Without further purification the crude material was dissolved in 15 ml of acetone and stirred with 407 mg (1.26 mmoles) of tetra-*n*-butylammonium bromide and 92 mg (0.86 mmoles) of 2,6-lutidine for 2 hours at 50°C . The solvent was removed in vacuo, a mixture of 30 ml of ether-water was added to the reaction mixture, and the ether layer was separated. The aqueous layer was extracted with another 20-ml portion of ether. The ether layers were combined and dried. After removal of the solvent in vacuo, the residue was chromatographed on 5 g of silica gel to afford 117 mg of colorless oil (5 and 10 percent ether in hexane). The oil was distilled under reduced pressure to give a pure sample of spiro enone 68 as a colorless oil: bp $90-100^\circ\text{C}$ (bath temperature)/0.2 mm; ir (CCl_4) 1734 cm^{-1} (cyclopentanone); nmr (CCl_4) δ 1.16 (d, $J = 5$ Hz, 3H, $-\text{CH}-\text{CH}_3$), 1.59 (br. s, 3H, vinyl CH_3) and 5.44 (br. s, 1H, vinyl H).

Anal. Calculated for $\text{C}_{12}\text{H}_{18}\text{O}$: C, 80.84; H, 10.18. Found: C, 80.87; H, 10.19.

Reaction of the Dihydrolumipproduct 47 with Hydrogen

Bromide Followed by Dehydrobromination

To a solution of 50 mg (0.309 mmoles) of dihydrolumipproduct 47 in 5 ml of ether was added 0.2 ml of 32 percent hydrogen bromide in acetic acid slowly with stirring. The reaction mixture was stirred in room temperature for 5 min. and then neutralized with 5 percent aqueous sodium bicarbonate. The ether layer was separated and dried. After

removal of the solvent in vacuo, the crude product was obtained as a yellow oil. The structure 69 was assigned according to its ir and nmr spectra: ir (CCl_4) 1747 cm^{-1} (cyclopentanone $\text{C}=\text{O}$); nmr (CCl_4) δ 1.81 (s, 3H, $-\text{CBr}-\text{CH}_3$).

Without further purification the bromo ketone was dissolved in 5 ml acetone and stirred with 155 mg (0.481 mmoles) of tetra-n-butylammonium bromide and 35 mg (0.327 mmoles) of 2,6-lutidine at 50°C for 2 hours. The solvent was removed in vacuo, a mixture of 30 ml of 1:1 ether-water was added to the reaction mixture, and after shaking the ether layer was separated. The aqueous layer was extracted with another 20-ml portion of ether. The ether layers were combined and dried. The solvent was removed in vacuo and the residue was chromatographed on 2 g of silica gel to afford 34 mg of a colorless oil (hexane and 5 percent ether in hexane). Distillation of this oil under reduced pressure gave a pure sample of spiro enone 70 as a colorless oil: ir (CCl_4) 1737 (cyclopentanone); nmr (CCl_4) δ 1.67 (br. s, 3H, vinyl CH_3) and 5.48 (br. s, 1H, vinyl H).

Anal. Calculated for $\text{C}_{11}\text{H}_{16}\text{O}$: C, 80.43; H, 9.83. Found: C, 80.49; H, 9.85.

Reaction of Dihydrolumipproduct 49 with Hydrogen

Bromide Followed by Dehydrobromination

To a solution of 50 mg (0.28 mmoles) of dihydrolumipproduct 49 in 2 ml of glacial acetic acid was added 0.2 ml of 32 percent hydrogen bromide in acetic acid slowly with stirring at room temperature. The reaction mixture was stirred for 5 min. and then 10 ml of ether was

added. After shaking, the ether layer was separated and washed with 5 percent sodium bicarbonate to remove the acetic acid. The ether layer was separated and dried. Following removal of the solvent in vacuo, the crude yellow oil obtained was assigned the bromo ketone structure 71 according to its spectral properties:

ir (CCl_4) 1720 cm^{-1} (cyclohexanone); nmr (CCl_4) δ 1.08 (d, $J = 6\text{ Hz}$, 3H) and 1.15 (s, 3H, angular CH_3).

Without further purification the bromo ketone was dissolved in 5 ml of acetone and stirred with 135 mg (0.415 mmoles) of tetra-n-butylammonium bromide and 31 mg (0.286 mmoles) of 2,6-lutidine for 2 hours at 50°C . After cooling to room temperature the solvent was removed in vacuo, and a mixture of 20 ml of 1:1 ether-water was added in the reaction mixture. The ether layer was separated and dried and the solvent was removed to yield 43 mg of yellow oil which was found to be a mixture of at least three products by glc (19). The major fraction accounting for more than 70 percent of the total product was isolated by preparative glc collection (22). Enone 72 (17 mg) was obtained by this method as a colorless oil: ir (CCl_4) 1714 cm^{-1} (cyclohexanone); nmr (CCl_4) δ 1.02 (s, 3H, angular CH_3) and 1.69 (s, 3H, vinyl CH_3). These spectral properties were found to be identical with those of compound 72 reported by Marshall (36).

Reaction of the Dihydrolumipproduct 48 with Boron Trifluoride Etherate in Benzene

A solution of 25 mg of compound 48 in 5 ml of benzene was treated with 50 mg of boron trifluoride etherate and the mixture was stirred at

reflux for 50 min. After cooling to room temperature the reaction mixture was then extracted with two 5 ml portions of water. The organic layer was dried and the solvent was removed in vacuo. The crude product was distilled under reduced pressure to give 11 mg of a colorless oil which was found identical to the enone 50 by comparison of nmr and glc (19) properties.

Reaction of the Dihydrolumipproduct 49 with
Boron Trifluoride Etherate in Various Solvents

A solution of 250 mg of compound 49 in 10 ml benzene was stirred with 100 mg of boron trifluoride etherate at reflux for 30 min. The reaction mixture was cooled to room temperature and washed with 20 ml of 5 percent aqueous sodium bicarbonate and dried. The solvent was removed in vacuo to give 250 mg of a dark oil. Four products were found in the order of retention time in a ratio of ca. 1:5:4:10 by glc (19). Yields were determined as 3, 13, 10 and 26 percent for the four products by using benzophenone as internal standard. The relative glc response factors of compounds 73 and 75 were determined by making a solution consisted of 10 mg of 73, 10 mg of 75 and 10 mg of benzophenone in 0.5 ml of acetone and measuring their peak areas shown on glc. For both compound 73 and compound 75, the response factors were found as ca. 0.95. Yields were calculated based on the assumption that compound 72 and compound 74 had the same response factor as compound 73 and/or compound 75.

A second run with 30 mg of 49 and 100 mg (Eq. 4.2) of boron trifluoride etherate under the same conditions gave the same four

products in a ratio of 3:3:6:8 by glc (19). Yields were determined in the same way to be 10, 10, 20 and 26 percent respectively. A third run using 50 mg of 49 with 250 mg (6.3 eq.) of boron trifluoride etherate in 5 ml of ether at reflux for 2 hours gave the same four products in a ratio of 9:2:4:5 by glc (19). Yields were determined the same way to be 31, 7, 15 and 18 percent respectively.

The four products were collected separately through preparative glc (22) at 165°C as colorless oils. The shortest retention time compound was found to be identical with compound 72 obtained before by comparing the glc and spectral properties. The second compound in order of retention time was found to be a colorless oil and identical with the compound reported as 73 (37) by comparing its spectral properties: uv max (MeOH) 240 nm (ϵ 11,000); ir (CCl_4) 1676 (α,β unsaturated C=O) and 1610 cm^{-1} (conj. C=C); nmr (CCl_4) δ 1.08 (d, $J = 6.5$ Hz, 3H, $-\text{CH}-\text{CH}_3$), 1.22 (s, 3H, angular CH_3) and 5.66 (br. s, 1H, vinyl H). The third compound was found to be a colorless oil and was assigned structure 74 according to its spectral properties: ir (CCl_4) 1713 (C=O) and 1600 cm^{-1} ; nmr (CCl_4) δ 0.79 (d, $J = 6.5$ Hz, 3H, $-\text{CH}-\text{CH}_3$), 1.18 (s, 3H, angular CH_3) and 5.83 (br. s, 1H, vinyl H).; the exact mass determination was calculated as 178.13576 and found as 178.13556. The fourth compound was found to be a colorless oil and identical to the compound reported as 75 (34) by comparison of the spectral properties: ir (CCl_4) 1678 (α,β unsaturated C=O) and 1611 cm^{-1} ; nmr (CCl_4) δ 0.92 (unresolved d, 3H, $\text{CH}-\text{CH}_3$), 1.10 (s, 3H, angular CH_3) and 5.64 (br. s, 1H, vinyl H).

4,4a,5,6,7,8-Hexahydro-4a,5a-dimethyl-
2(3H)-naphthalenone (75)

A solution of 6.3 g (0.050 moles) of 2,3-dimethylcyclohexanone and 2.3 g (0.051 moles) of 53 percent sodium hydride in 250 ml of DMSO was stirred at room temperature for 2 hours. A solution of 3.5 g (0.051 moles) of methyl vinyl ketone in 100 ml of DMSO was added dropwise with stirring. The reaction mixture was stirred at room temperature for 3 hours and then neutralized with 5 percent hydrochloric acid. The mixture was extracted with three 200-ml portions of hexane and the hexane layers were combined and dried. The solvent was removed in vacuo to give a brown oil containing some residual DMSO. Distillation of the brown oil under reduced pressure gave 1.27 g of a pale yellow oil (bp 120-130°C/0.2 mm). This oil was found to be a mixture of 75 and 77 in a ratio of ca. 4:1 by glc (19). Preparative glc collection of the oil gave a colorless oil containing more than 90 percent 75 which was found to have identical spectral properties with those reported (35). The nmr spectrum was found to be identical with the spectrum of pure 75 kindly supplied by Dr. Pinder (34).

Hydrogenation of Lumiprodukt 33

A solution of 145 mg (0.670 mmoles) of 33 in 0.5 ml of anhydrous ethanol was injected into a reaction mixture prepared by stirring 15 mg of 5 percent palladium on carbon in 5 ml of anhydrous ethanol for 2 hours under hydrogen at atmospheric pressure. The absorption of hydrogen was observed immediately and interrupted after one equivalent (16.4 ml) of hydrogen was taken up. After removal of the catalyst by

filtration and removal of the solvent in vacuo, the crude product was distilled under reduced pressure to give 128 mg of a colorless oil 76: bp 115–120°C (bath temperature)/0.2 mm; ir (CCl₄) 1717 cm⁻¹ (C=O); nmr (CCl₄) δ 1.15 (d, J = 6 Hz, 3H, -CH-CH₃), 1.33 (s, 3H, angular CH₃) and 1.60 (br. s, 6H, =C(CH₃)₂). The exact mass determination was calculated as 218.1671 and found as 218.1675.

Attempted Acid Ring Opening of Dihydrolumipproduct 76
with Boron Trifluoride Etherate

A solution of 100 mg of 76 and 100 mg of boron trifluoride etherate in 10 ml of benzene was stirred at 65°C for 50 min. After being allowed to cool to room temperature the reaction mixture was extracted with 10 ml of water twice. The organic layer was separated and dried. The solvent was removed in vacuo to yield 87 mg of a brown oil. This crude product was found to be a mixture of at least four components by glc (19) and none of them corresponded to the desired ketones 28 or 35. Further identification of the products were not successful.

Attempted Acid Catalyzed Isomerization of Spiro Enone
68 with Boron Trifluoride Etherate in Benzene

A solution of 25 mg of spiro enone 68 and 25 mg of boron trifluoride etherate in 5 ml of benzene was stirred at reflux for 50 min. The reaction mixture was neutralized with 5 percent sodium bicarbonate. After separation the aqueous layer was extracted with two 5 ml portions of ether. The organic layers were combined and dried. The solvent

was removed in vacuo. The recovered material showed identical properties to those of the starting material.

Hydrogenation of Enone 72

A solution of 17 mg of enone 72 and 2 mg of 5 percent palladium on carbon in 2 ml of anhydrous ethanol was hydrogenated in the same way as described for 33. The same work up gave an oil which showed one peak in glc analysis (19) with spectral properties corresponding to the dihydro compound 78: nmr (CCl_4) δ 0.87 (s, 3H, angular CH_3), ir (CCl_4) 1709 cm^{-1} (cyclohexanone) and exact mass determination 180.1508 (calculated 180.1514).

Hydrogenation of Enone 74

A solution of 10 mg of sample mainly enone 74 and 1 mg of 5 percent palladium on carbon in 2 ml of anhydrous ethanol was hydrogenated in the same way as described for 33. The same work up gave an oil which was found to be a mixture of two products by glc (19). The major peak accounting for more than 90 percent of the mixture (with retention time 6.5 min.) was found to be identical with 78 by comparison of its spectral properties.

CHAPTER IV

DISCUSSION OF RESULTS

As stated in the first chapter, this research was devoted to a study of the synthesis and photochemical interconversion of cross-conjugated cyclohexadienones related to α - and β -vetivone. To accomplish this goal a simple ketone 50 was first synthesized and studied as the model compound. Because of its availability, nootketone was used as the source of α -vetivone and the corresponding cross-conjugated dienone.

Both enone 50 and its isomer enone 51 were prepared stereoselectively by the procedure of Scanio and Starrett (17). The stereoselectivity was observed to be solvent dependent. In dioxane more than 90 percent of the annelation product was enone 50. In this solvent it was considered that in the Michael addition reaction the transition state 79 leading to the cis-dimethyl product should be favored from a steric and an electronic point of view (27). In the highly polar solvent DMSO a sequence involving an aldol condensation followed by a thermally allowed disrotatory cyclization was suggested (17) (Chart 7) to explain the fact that 95 percent of the enone was trans-dimethyl compound 51. The identification of enone 50 and 51 was based upon different absorptions in the nmr spectra of the two compounds. The angular methyl group of enone 50 has a singlet at δ 1.05 whereas enone 51 has a singlet at δ 1.26 (17).

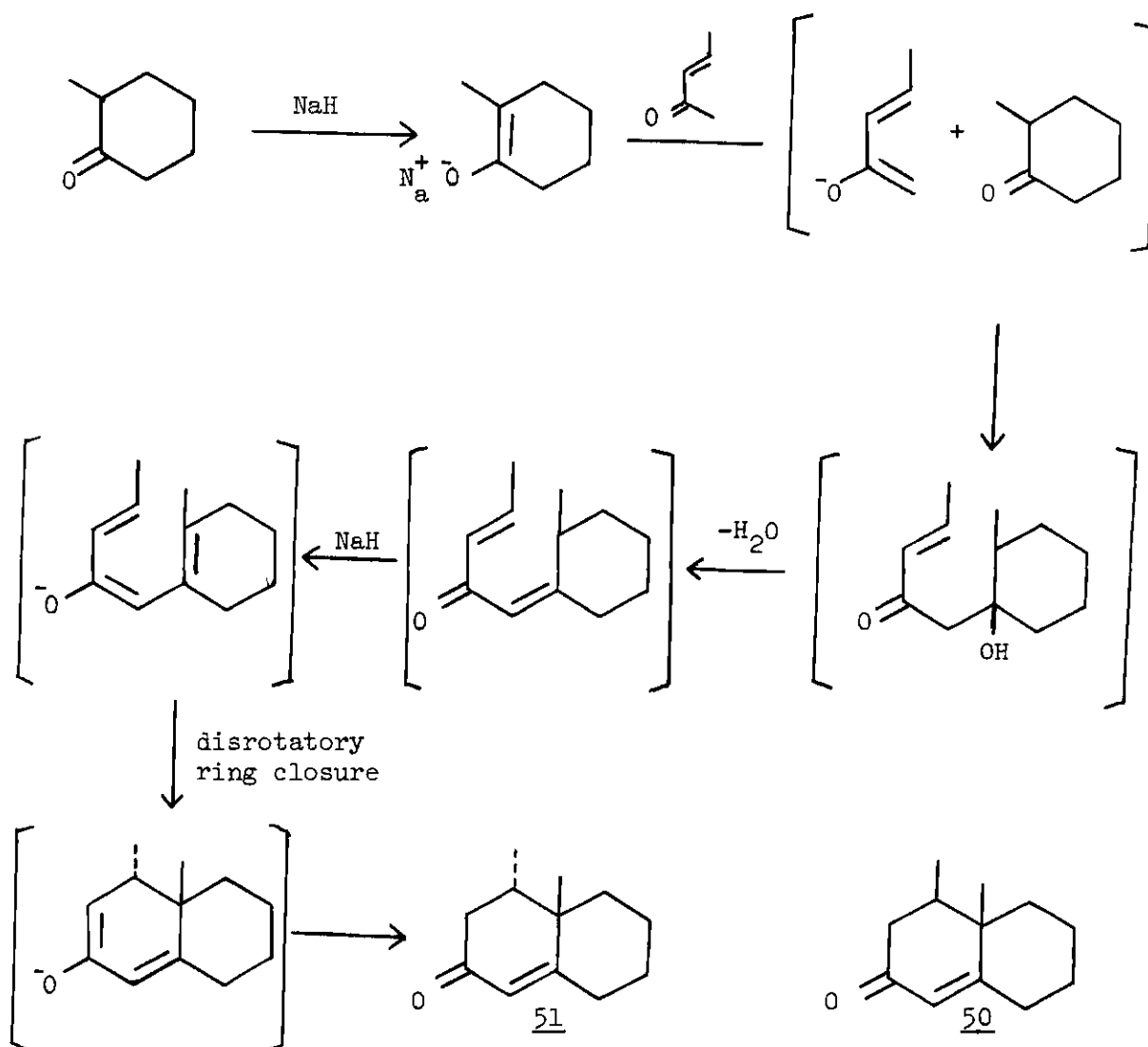
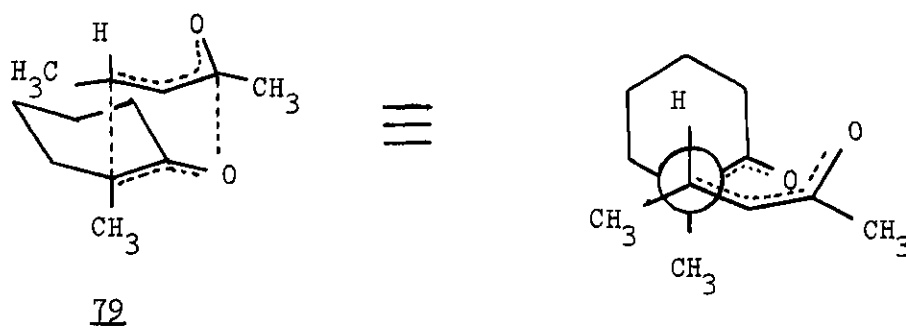


Chart 7. Mechanism of the Stereoselective Synthesis of Enone 51

Cross-conjugated dienone 52 was obtained via oxidation of either 50 or 51 with DDQ. The enone 50 with axial hydrogen atom at C-4 was expected to be more reactive than enone 51 in this oxidation. Actually the yields of 52 were found not to differ greatly being 39 and 34 percent from 50 and 51, respectively. In these cases, as with other 4-methyl substituted dienones prepared later, the reaction was incomplete and column chromatography was required to separate the dienone from the starting enone. The ultraviolet absorption maximum at 245 nm and the infrared absorption at 1667 cm^{-1} suggested the presence of α,β -unsaturated ketone. The nmr spectrum agreed the structure 52 since it showed one vinyl methyl, one angular methyl, and two vinyl hydrogens.

It was expected that irradiation of 52 in anhydrous dioxane would yield the lumipproduct 53 (see Chart 9). The dioxane used in all irradiations was dried by reflux over sodium metal and freshly distilled immediately prior to use. Unlike the C-4 unsubstituted compound, this dienone gave incomplete conversion on ultraviolet irradiation under various conditions. Separation of the photoproduct from the starting material on column chromatography was also required. The yields were found to be around 60 to 70 percent. Best results were obtained when the temperature of the dioxane solution was maintained at 20-25°C during the photolysis. The spectral properties of 53 were consistent with the structural assignment. The ultraviolet absorption maximum at 234 nm and infrared spectrum at 1695 cm^{-1} indicated the presence of α,β -unsaturated ketone in five-membered ring and conjugated with a three-membered ring. Its nmr spectrum revealed the correct expectation with

one angular methyl group at δ 1.15, one methyl group at δ 1.97, and one vinyl hydrogen at δ 5.50.

Isolation of spiro dienones of the type 54 was one of the purposes of this research. This was successfully performed by irradiation of 53 in 45 percent aqueous acetic acid using a broad spectrum lamp fitted with Pyrex filter. In previous reports in which the isolation spiro dienones were attempted (6,8), the irradiations were carried out in a quartz apparatus. Pyrex is opaque to light of wavelength shorter than 3000 \AA . Thus dienones such as 54 are apparently stable to the light of wavelength greater than 3000 \AA . To prove this point, the irradiations of lumiprodukt 62 with light filtered through both Pyrex and quartz were carried out. The results showed that the irradiation with the Pyrex filter gave exclusively spirodienone 63 while the irradiation with the quartz filter went all the way to the phenolic compound 64. The spirodienone 63 was also observed to isomerize thermally to the compound 64. (Chart 8).

For spiro dienone 54, the ultraviolet absorption maximum at 245 nm and infrared spectrum at 1668 cm^{-1} agreed to the presence of α, β unsaturated ketone while the nmr spectrum showed strong support with two identical methyl groups at δ 2.01 and two identical vinyl hydrogens at δ 5.90. The mechanism of a photo-induced cleavage of 1,8a-bond followed by rearrangement of methylene group (Chart 9) in steroid enones (28), can be applied to spiro dienone formation. Isolation of intermediate in our work substantiates this mechanism.

Nootkatone is a mildly pungent sesquiterpene ketone valued

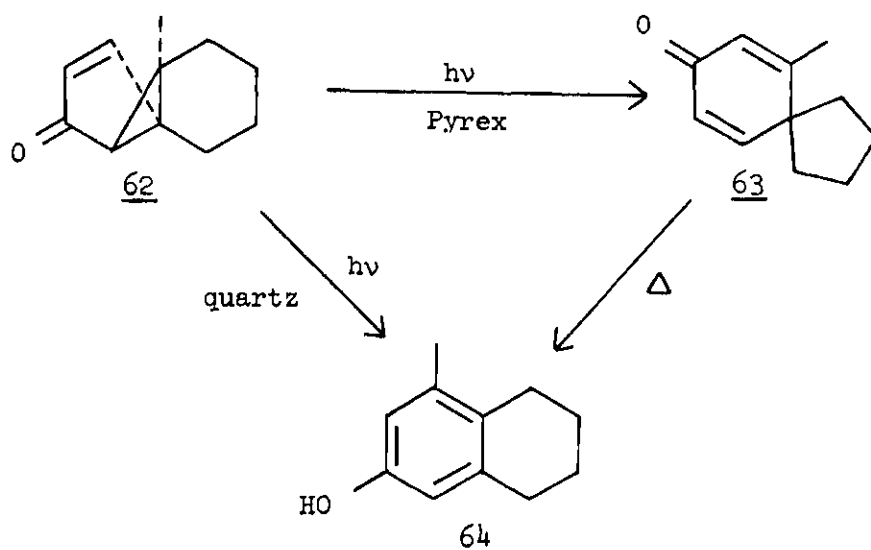


Chart 8. Photolysis of Lumiprodukt 62

for its contribution to the distinctive flavor of grapefruit (Citrus paradisi), especially in the essential oil pressed from the peel (28). It was characterized (29) originally as a heartwood constituent of Alaskan yellow cedar (Charaecyparis nootkatensis) and formulated as either 80 or 81. The correct structure was proven as 30 by Macleod (12).

3,4-Dehydronookatone 32 was prepared through oxidization of nootkatone with DDQ as reported (12). The physical properties of the final product well support the structure 32. The ultraviolet absorption

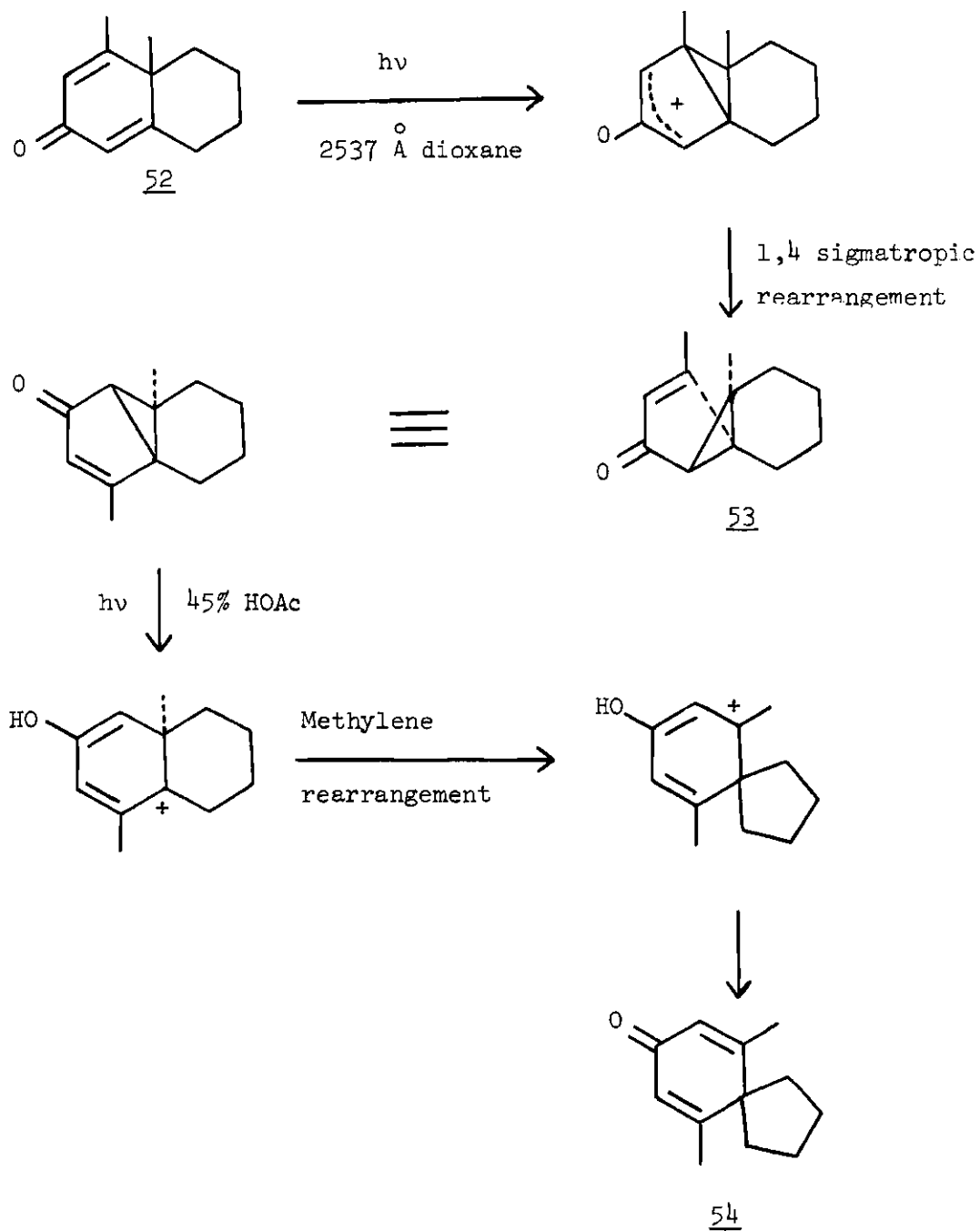
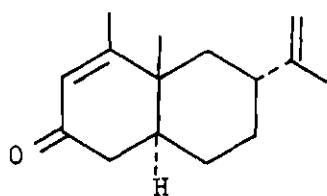
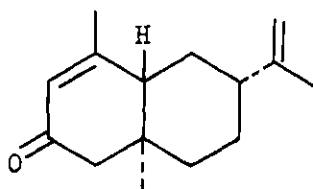
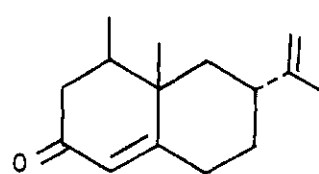


Chart 9. Photolysis of Dienone 52 in Anhydrous Dioxane at 2537 Å

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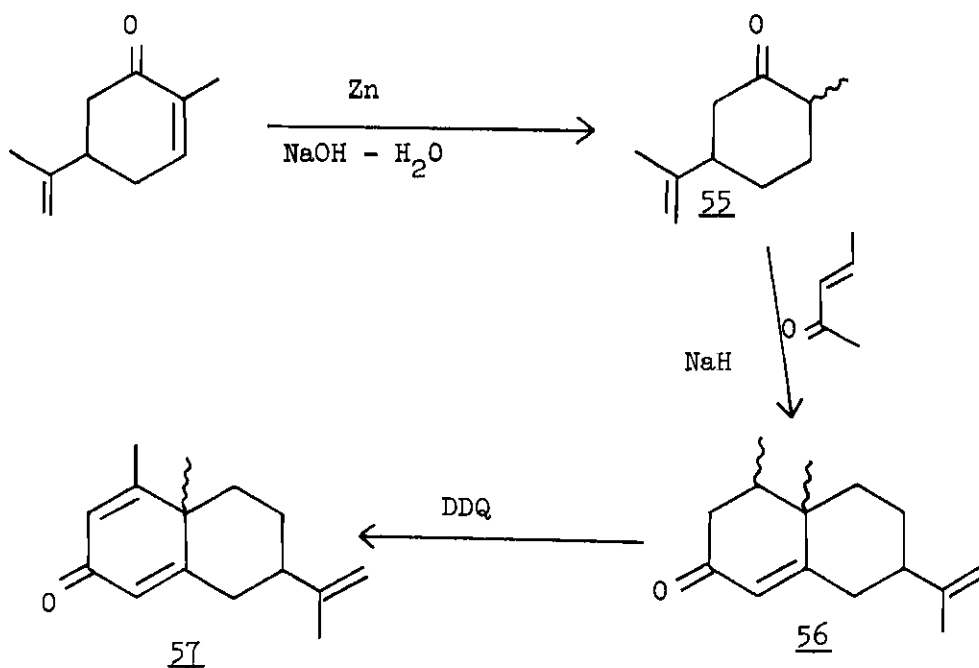
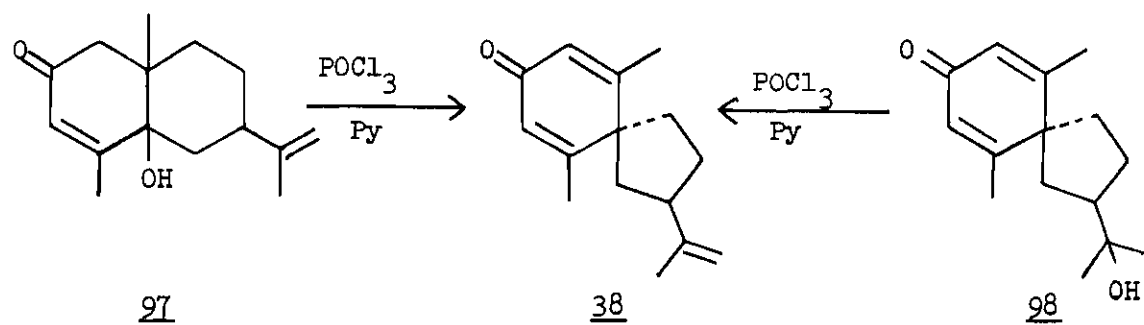
maximum at 244 nm and infrared absorption at 1660 cm^{-1} (CCl_4) indicated the presence of α,β unsaturated ketone whereas the nmr spectrum (CCl_4) showed one saturated methyl group at δ 1.35, two different vinyl methyl groups at δ 1.72 and 1.98 and two groups of two vinyl hydrogens at δ 4.73 and 5.95.

The lumipproduct 36 was prepared in the same way as 53. The spectral properties of the purified product yield the structure assigned. The ultraviolet absorption maxima at 234 nm and 268 nm and the infrared absorption maxima at 1682, 1610 and 892 cm^{-1} indicated the presence of the α,β unsaturated carbonyl group which also cross-conjugated with a three-membered ring. The nmr spectrum showed the presence of one angular methyl group, two different vinyl methyl groups, and two different groups of vinyl absorptions, one for terminal methylene group on the side chain with two hydrogens and the other as a single hydrogen on the position of the ring.

Further irradiation of the lumipproduct 36 in 45 percent aqueous acetic acid gave three products in 12, 36 and 45 percent yields. These yields were determined by the glc (19) peak area measurement using benzophenone as internal standard. The first product in order of

retention times by glc (19) was found identical to 3,4-dehydronootkatone (32) by comparing their uv, ir, and nmr spectra. The second product was found to show a similar nmr spectrum as 32 with one angular methyl group absorption at δ 1.32, two different vinyl methyl group absorptions at δ 1.78 and 1.99, a terminal methylene group absorption at δ 4.78 and two vinyl hydrogen absorptions at δ 5.97. Its ultraviolet absorption maximum at 245 nm and infrared absorption maximum at 1668, 1631, and 898 cm^{-1} agreed the presence of an α,β unsaturated carbonyl group in the assigned structure 37. The high resolution mass spectrum and carbon hydrogen analysis also supported the structure. The direct proof of the structure came from an alternative synthesis which yielded 37 as a minor product. This synthesis involved the ring annelation of 3-penten-2-one and dihydrocarvone (55) (21) followed by oxidation of the octalone product mixture 56 with DDQ (Chart 10). The first intermediate enone product was found to be a mixture of two isomers which in its nmr spectrum gave a similar pattern to nootkatone. This enone was oxidized with DDQ without further purification. The final product was found to be a mixture of two isomers in a ratio of 3:7 by glc (19). The minor product, with retention time 30.4 min. at a column temperature of 200°C (isothermal), was collected and found to be identical with the compound 37 isolated from the previous photoreaction.

By comparing uv, ir, and nmr spectra the third product was found to be identical with the compound anhydro- β -rotunol prepared by Hikino and coworkers (20a, 30) through dehydration of β -rotunol 97 or dienone 98 with phosphorous oxychloride in pyridine (Chart 11). The high

Chart 10. Synthesis of Trienone 57Chart 11. Alternative Synthesis of Spiro Trienone 38

resolution mass spectrum and carbon hydrogen analysis also supported the structure 38.

The identity of a new natural product, isolated from a Solanum species and having the spirovetiva-1 (10), 3, 11-trien-2-one structure was proved by Coxon (31) upon comparison of spectral and other physical data of compound 38 with this new product.

In the irradiation of 36, the carbonium ion 82 appears to be a reasonable intermediate leading to these products. The initial photo-induced cleavage of the cyclopropyl ring gives this species. Migration of the methyl group in 82 and loss of a proton yield 37 while migration of the methylene group and proton loss can give 38 (Chart 12). Compound 32 is found to be a secondary product from both 37 and 38 as will be discussed later. When the irradiation of 36 was carefully monitored by glc (19), it was found that the initial ratio of the methyl to methylene migration products (i.e. 37 to 38) was 3:7.

Compounds 37 and 38 were isolated and their photochemical behavior was investigated. The direct irradiation of 37 with a high-pressure mercury lamp in 45 percent aqueous acetic acid for 60 min. gave a mixture of 32, 37 and 38 in a ratio of 1:3:2. This reaction was further studied by irradiating 37 with low pressure mercury lamp in anhydrous dioxane for 6 hours. This gave a new product having a glc retention time similar to that of the lumiprodukt 36. The structure 83 was assigned for this intermediate. Without complete characterization this compound was irradiated for 30 min. in 45 percent aqueous acetic acid with a high-pressure mercury lamp as described for dehydroluminoot-

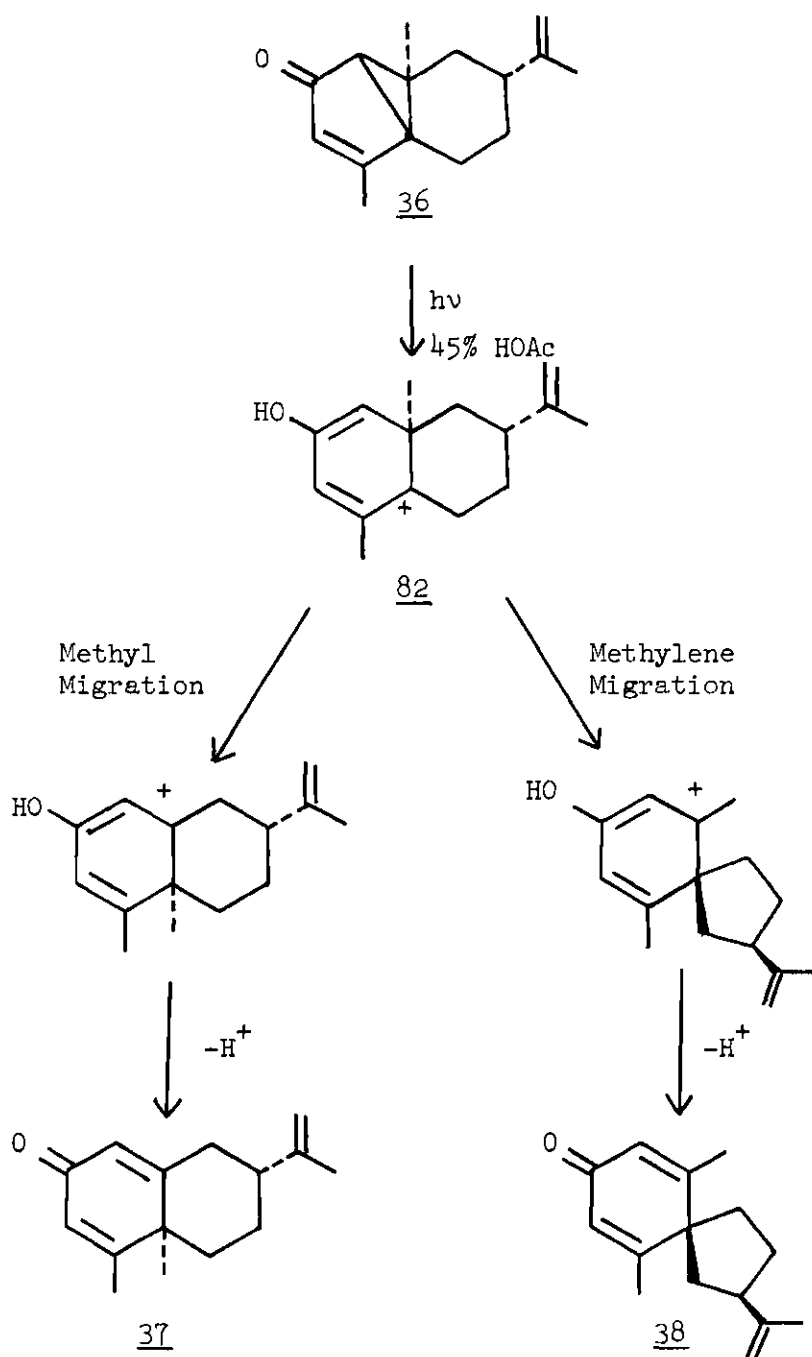


Chart 12. Methyl vs. Methylene Migration in Reactions of Lumiprodukt 36

katone (36) to give a mixture of 32, 37 and 38 in a ratio of 2:2:3 (Chart 13). The initial ratio of the methyl to methylene products, which rearranged through intermediate 84, was found to be 15:85 when the photolysis was monitored by glc (19).

The direct irradiation of 38 with high pressure mercury lamp in 45 percent aqueous acetic acid for 60 min. gave a mixture of 32, 37 and 38 in a ratio of 2:3:2 according to glc (19). The irradiation of 38 in dioxane for 6 hours with a low pressure mercury lamp gave a group of four compounds with short retention times compared with the starting material were assigned the diastereometric structures 85, 86, 87 and 88 because their glc retention times were similar to that of 36. Without separation and characterization, this mixture was irradiated 30 min. with a high pressure mercury lamp in 45 percent aqueous acetic acid to give a mixture of 32, 37 and 38 in a ratio of 2:3:2. This suggested a mechanism which involves first formation of lumiproducs 85, 86, 87 and 88, followed by a photo-induced cleavage to intermediates 89 and 90 which may rearrange thermally to possible products of structures 32, 95, 96, 37. (Charts 14 and 15). Only two of the possible four isomers, that is, 32 and 37 were found as products and showed an initial ratio of 1:1.

Examination of models of dienone structures 95 and 96, indicates that these species are unstable with respect to 32 and 37. In the two former isomers the isopropenyl side chain must be axial with respect to the B ring if only chair conformations are considered whereas in the latter cases the side chain is equatorial with respect to the B ring.

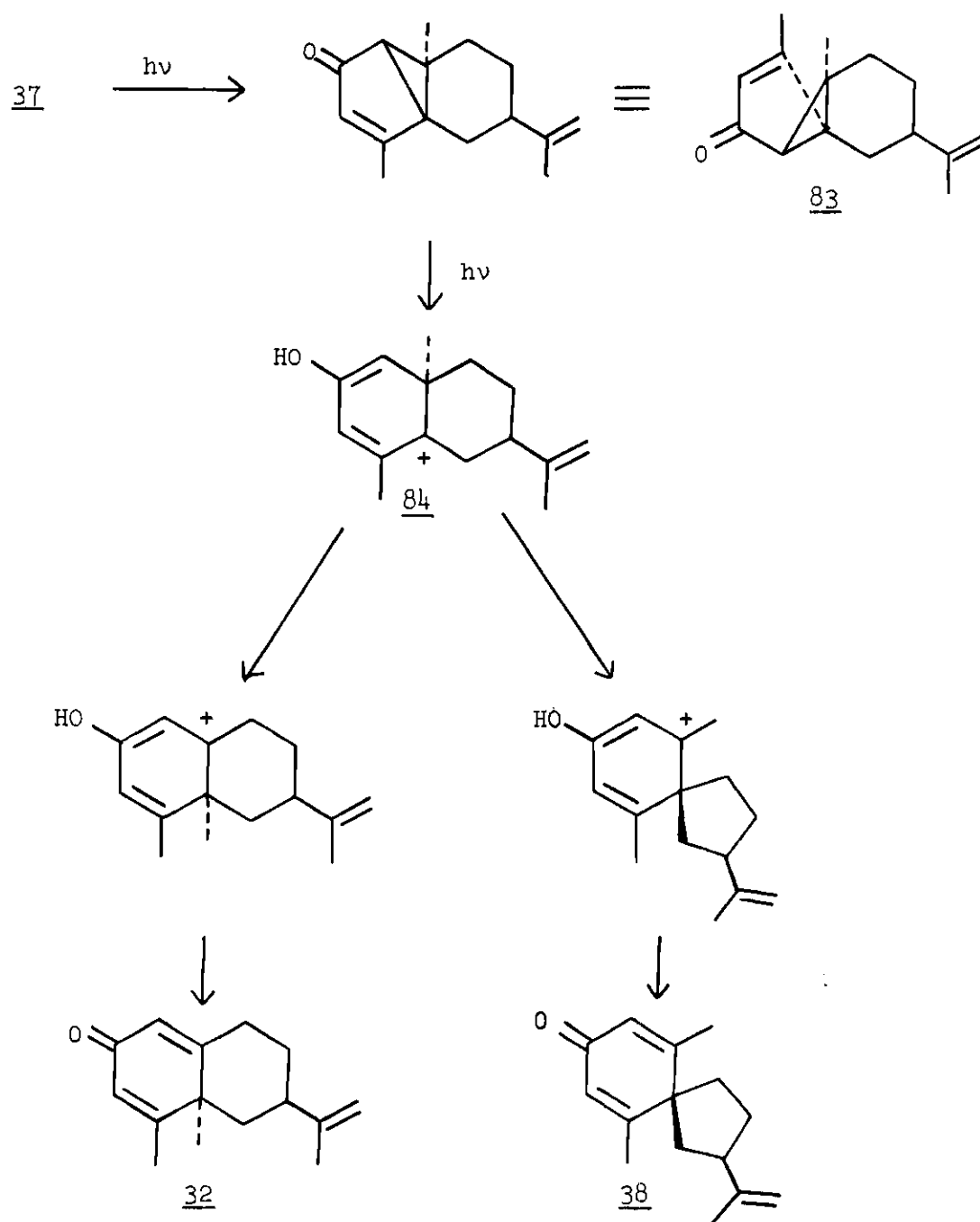


Chart 13. Irradiation of Trienone 37 in Dioxane and Aqueous Acetic Acid

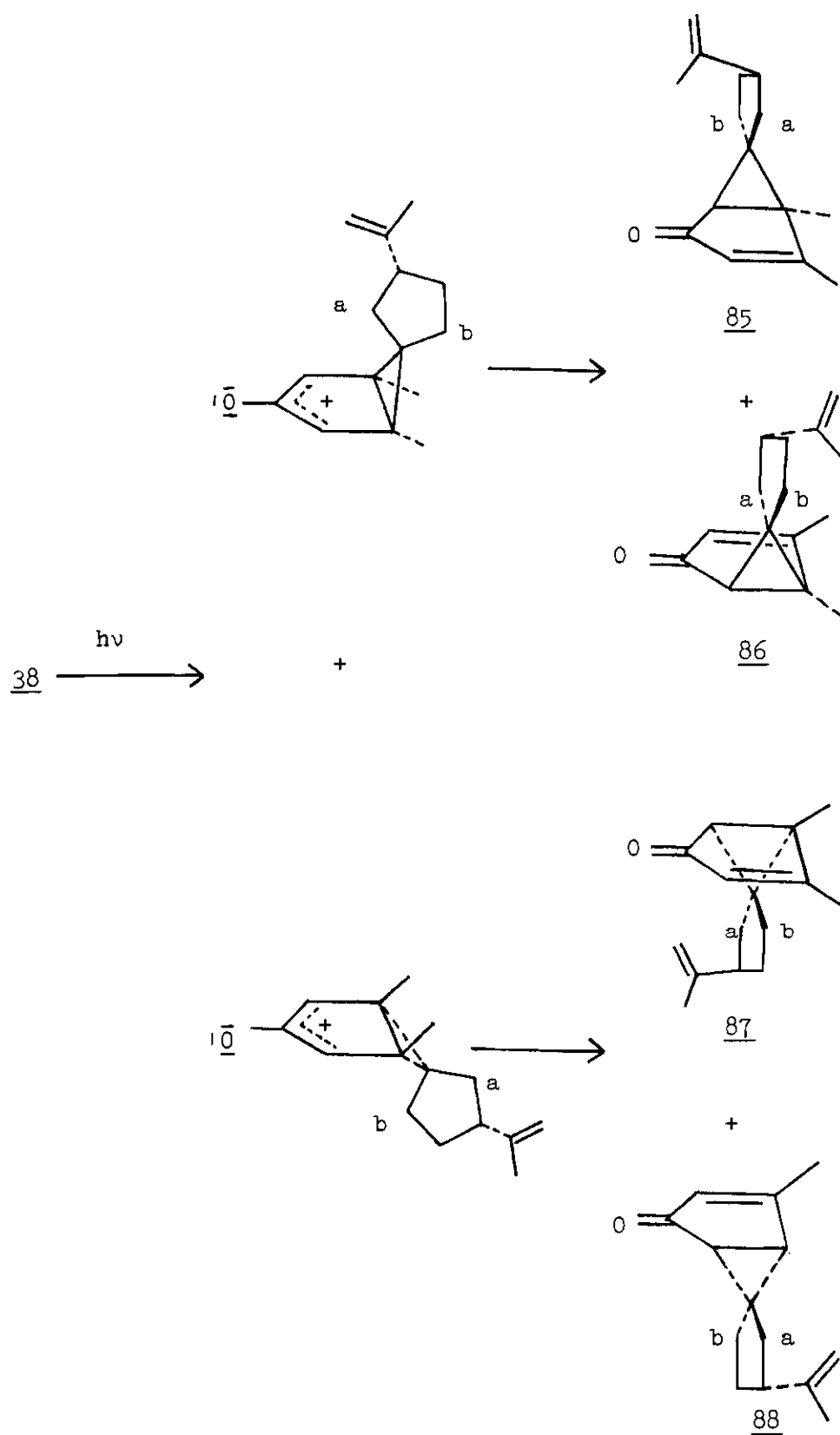


Chart 14. Irradiation of Trienone 38 in Dioxane and Aqueous Acetic Acid

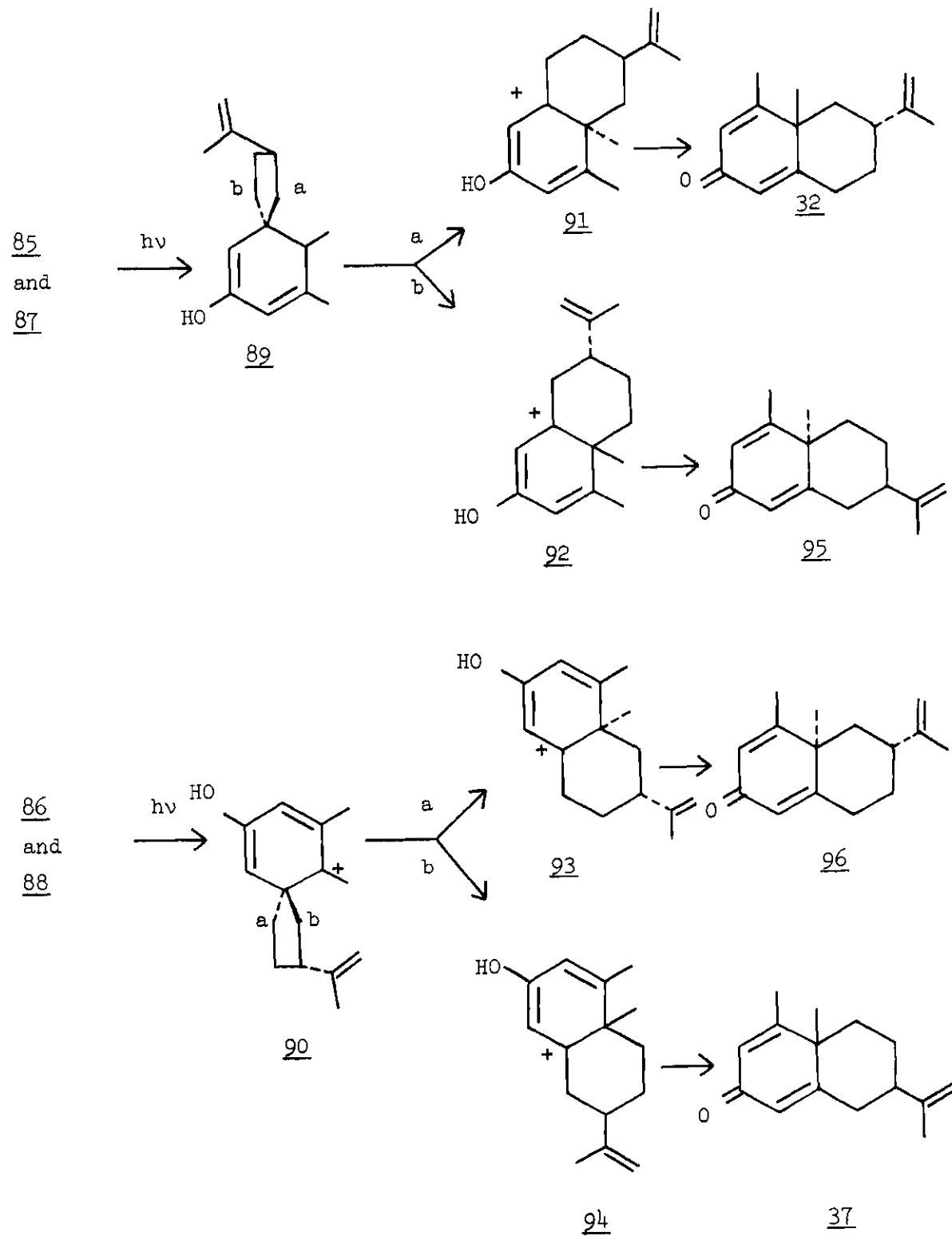
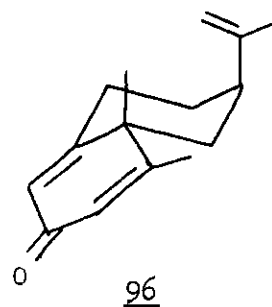
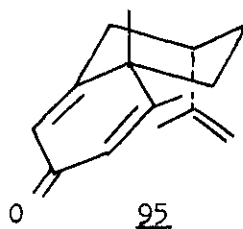
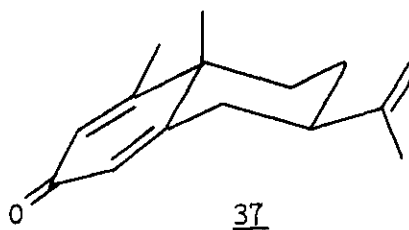
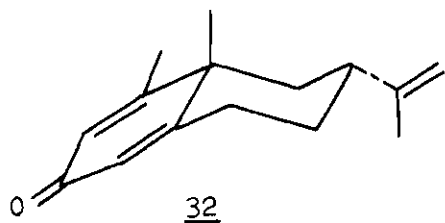


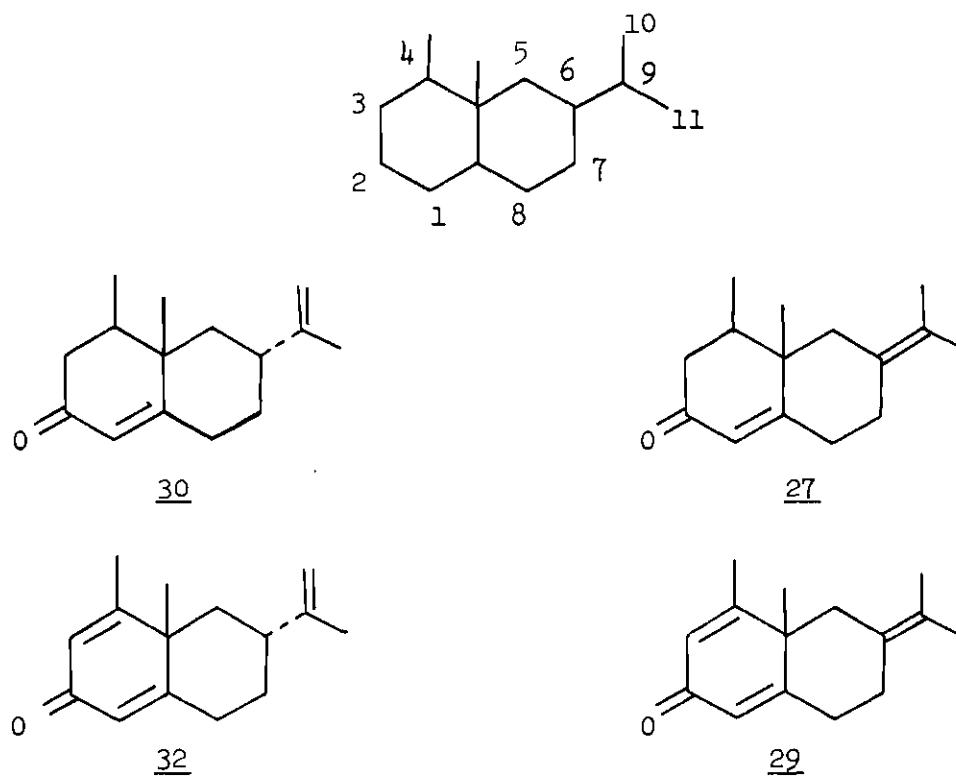
Chart 15. Irradiation of Trienone 38 in Dioxane and Aqueous Acetic Acid

Thus it is possible that the transition states leading to 95 and 96 from carbonium ions 89 and 90, respectively, are unstable with respect to the transition states which lead to 32 and 37. It also is possible that 95 and 96 are formed photochemically, but because of their relatively high energy are converted to the more stable dienones via the corresponding lumiprodukt intermediates.



Naturally occurring α -vetivone was isolated along with β -vetivone as the main ketonic compounds in the oil of vetiver (32a, 32b). Separation of α - and β -vetivone is difficult, preparative glc being required to isolate the pure materials. Thus other ways of obtaining α -vetivone were investigated. The conversion of nootkatone into α -vetivone was

found to be successful by isomerization of the 9,10-double bond to the 6,9-position either by refluxing in *p*-toluene sulfonic acid or by adding hydrogen bromide to 30 followed by dehydrobromination of the product with tetra-*n*-butylammonium bromide in acetone containing 2,6-lutidine (Chart 4). Both methods gave a mixture of 30 and 27 in a ratio of ca. 1:8 and the yields were generally in the 75 to 85 percent range. In the latter approach the weakly basic medium allows the production of the more thermodynamically stable tetra-substituted double bond (23).



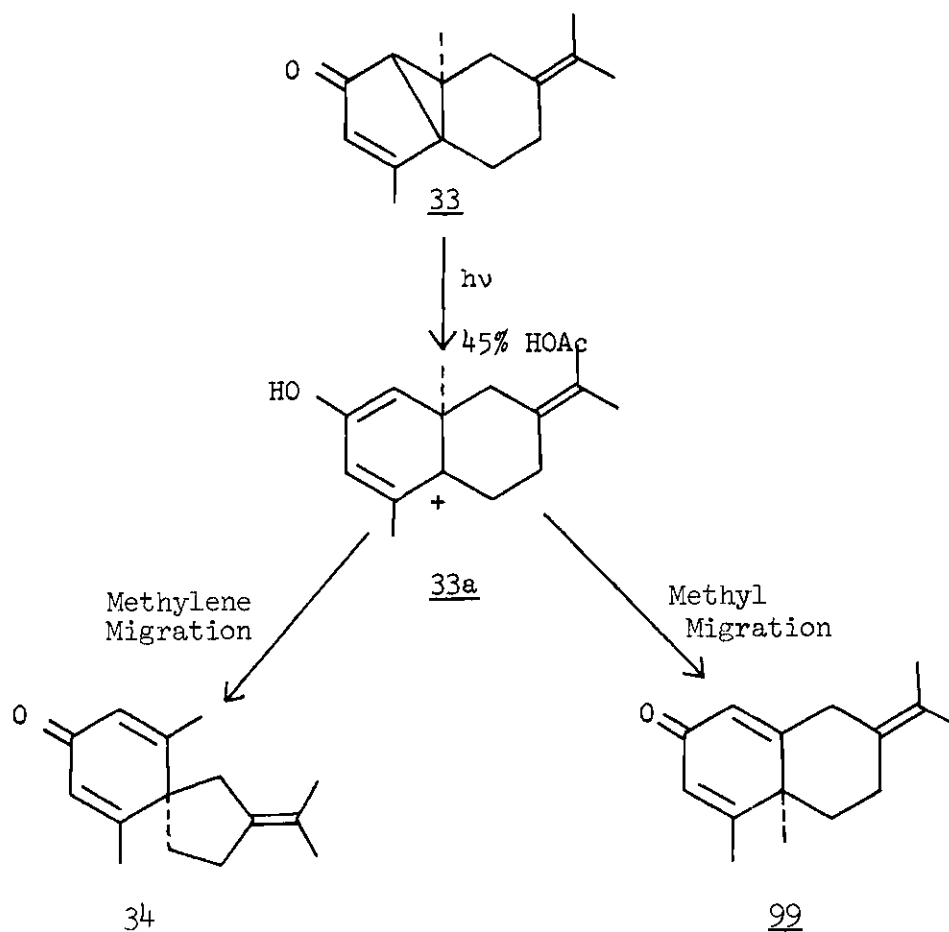
Dehydro- α -vetivone (29) was found as a minor product of oxidation of α -vetivone with DDQ (11). The conversion of dehydronookatone 32 to 29 was successfully carried out by addition of hydrogen bromide to give

32a as an intermediate followed by dehydrobromination with tetra-n-butylammonium bromide and 2,6-lutidine in acetone. The product was a mixture of 29 and 32 in a ratio of ca. 8:1 and separated by column chromatography using silver nitrate impregnated silica gel. The pure sample obtained was found to have identical properties to those reported (12).

Lumiproduct 33 was prepared from irradiation of 29 in dioxane at 2537 Å. The physical properties support its structure with a uv absorption maximum at 232 nm, an ir absorption maximum at 1685 cm⁻¹, and nmr absorptions at δ 1.16 (3H), 1.65 (6H), 1.98 (3H) and 5.47 (1H).

Irradiation of 33 under in the same conditions as described for 36 gave dehydro- β -vetivone 34 as the exclusive photoproduct in 50 to 60 percent yield. No evidence for the formation of a product such as 99 which would be derived from a 1,2-methyl migration in a carbonium ion intermediate 33a was obtained. Also, possible products of further rearrangement of 34 were not observed indicating that this compound is relatively stable to irradiation with long wave length light. The pre-dominate formation of 34 is suggested to be due to the greater migratory aptitude of an allylic methylene group over that of a methyl group.

The irradiation of 34 in dioxane at 2537 Å gave a mixture of two products whose glc behavior (19) and spectral properties (uv max at 227 nm, ir max at 1689 cm⁻¹, and nmr max at δ 1.40, 1.60, 1.97 and 5.40) indicated that it was composed of ca. 1:1 mixture of two racemic diastereomers as 58a and 58b. Irradiation of this mixture in aqueous acetic acid using Pyrex filtered light gave racemic dehydro- α -vetivone



(29) in ca. 50 percent yield from 34 (Chart 16). Migration of the allylic methylene group in the carbonium intermediates derived from 58a and 58b account for the formation of racemic 29.

In order to complete the conversion of nootkatone to a vetispirane derivative, selective reductions of dehydro- β -vetivone were carried out. Catalytic hydrogenation of 34 in ethyl alcohol at atmospheric pressure using 5 percent palladium on calcium carbonate as catalyst gave approximately 40 percent of saturated ketone 59 and 60 percent of a mixture of racemic β -vetivone 28 and racemic 10-epi- β -vetivone 35

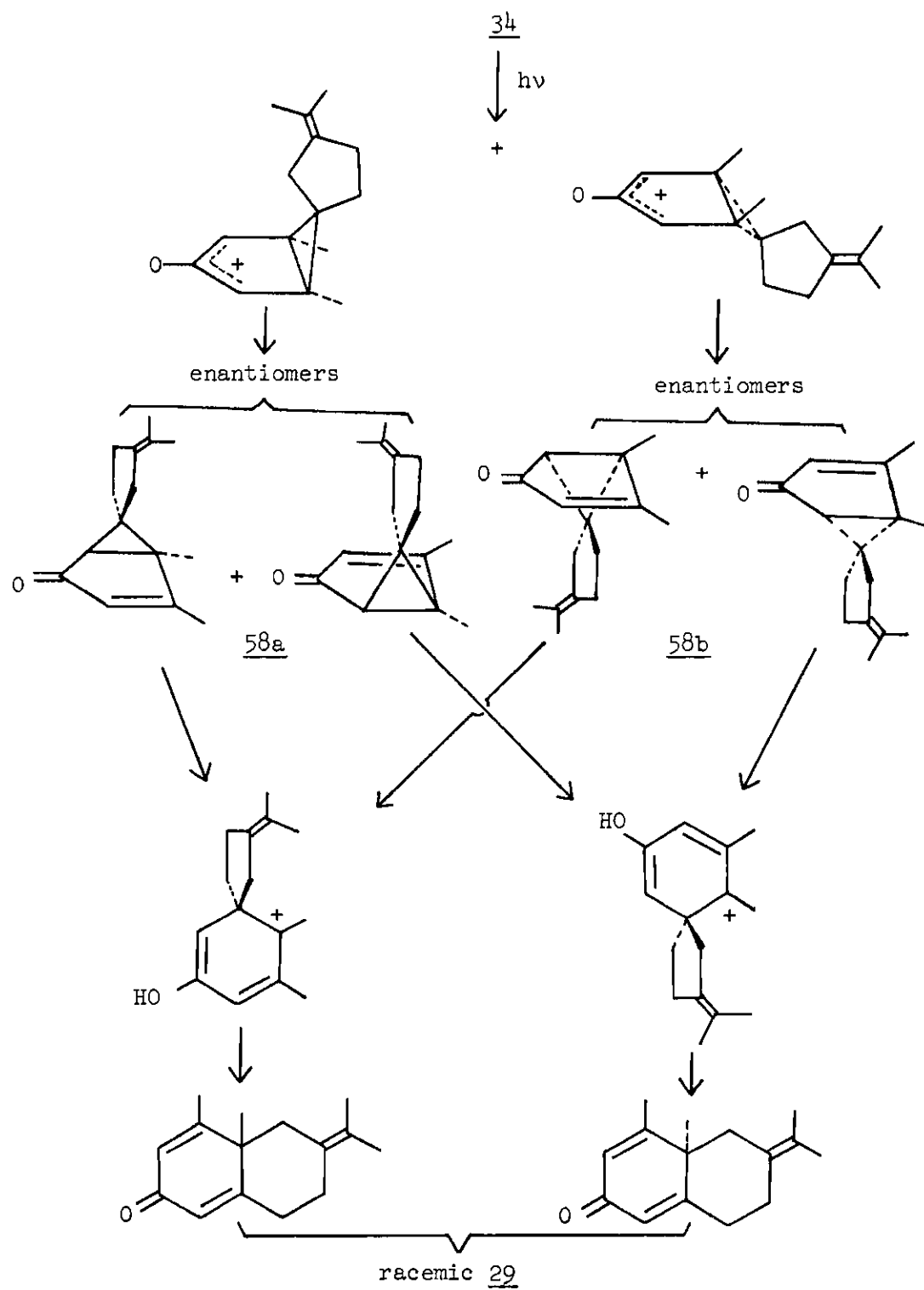
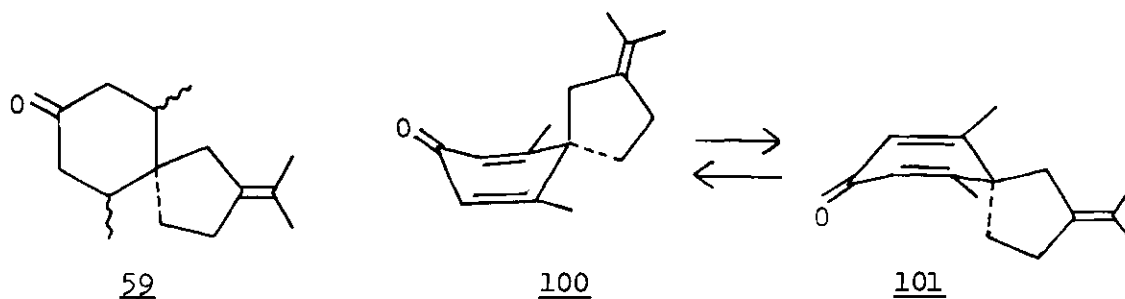


Chart 16. Rearrangement of Trienone 34

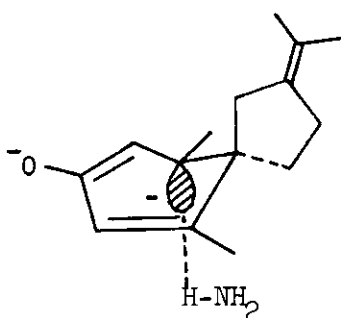
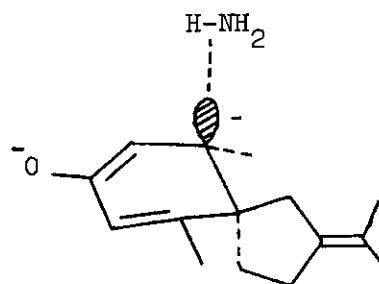
in a 7:3 ratio by glc (19). Chemical reduction of 34 with two equivalents of lithium in ammonia containing one equivalent t-butyl alcohol gave a mixture of 28 and 35 in ca. 80 percent yield. In this case the ratio of 28 to 35 was 3:7 by glc (19).

The spiro trienone 34 may exist in two possible conformations 100 or 101. Absorption of the molecule on a catalyst surface from the convex face of the boat form of ring A should take place preferentially. From examination of models it appears that the convex face (α side) of conformation 100 is slightly less hindered than the convex face (β side) of conformation 101 because in the latter one of the methyl groups of the isopropylidene group offers a small degree of steric hindrance to absorption on a flat surface. Thus there is a slight preference for the reduction of 34 from the α side of conformation 100 to produce somewhat more of racemic β -vetivone than its 10-epimer.



In the lithium-ammonia reduction of 34 the major product is 10-epi- β -vetivone (35). Structure 102 and 103 represent the two stereo-electronically allowed transition states for protonation at C-10 of the dianionic intermediate derived from 34. Transition state 102 would lead to β -vetivone while 103 would lead to its 10-epimer. The results of the

reduction suggest that there is a small preference for 103. However, examination of models does not reveal any obvious differences in the electronic or steric factors involved in the two transition states. Thus at this time we are not able to provide a good rationale for these reduction results.

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The hydrogenation of dehydro- α -vetivone to reform α -vetivone was not successful primarily due to the fact that the 1,8a-double bond was more susceptible to hydrogenation than the 3,4-double bond. Under a variety of reduction conditions dihydro- and tetrahydro derivatives of 29 were produced but no evidence for the presence of α -vetivone was found by comparison the glc chromatograms of reduction mixtures with that of an authentic sample of α -vetivone. The lithium-ammonia reduction of 29 gave a surprising result in that a phenolic product was obtained exclusively. This compound was assigned the structure 60 on the basis of the following spectral properties: ir max at 3610 (-OH), 1610, 1595, 1485 and 1456 cm^{-1} (aromatic) and nmr at δ 1.62 (three vinyl methyl group), 2.08, 2.16 (two aromatic methyl groups) and 6.42

(aromatic hydrogen).

The fact that a phenol was found from lithium-ammonia reduction of dehydro- α -vetivone and not from dehydro- β -vetivone is of interest. Dienone 29 can yield a dianionic species (104) which can undergo cleavage of the 4a,5-bond to give the resonance stabilized dianion 105. Addition of a proton from ammonia would yield a phenoxide which would give 60 on addition of ammonium chloride (Chart 17).

Examination of models of the stereoelectronically allowed dianionic intermediate 104 derived from dehydro- α -vetivone and the two possible dianionic species derived from dehydro- β -vetivone (cf. 102 and 103) shows that only the former case is the σ orbital of the C-C bond which undergoes cleavage in a position to overlap with the isopropylidene π -bond. Apparently, protonation at the β -position and intramolecular C-C bond cleavage are competitive processes in systems of this type and the isolation of 60 in the case of dehydro- α -vetivone is due to the above mentioned orbital overlap being sufficiently favorable for the cleavage reaction to take place (Chart 17).

As mentioned in the introduction, cleavage of a bicyclohexanone derivative such as 76 appeared to be a possible useful route to vetispirane derivatives (Chart 18).

The cleavage of 1,8a-bond could generate the carbonium ion (76a) which might be expected to undergo either a 1,2-methyl or 1,2-methylene shift to give products of the type 107 or 35, respectively. Huffman (33) has carried out studies in an effort to generate carbonium ions related to 76a. In his work the hydroxy enone 108 was dehydrated with phosphoryl chloride-pyridine to give the linear dienone 109 as the only

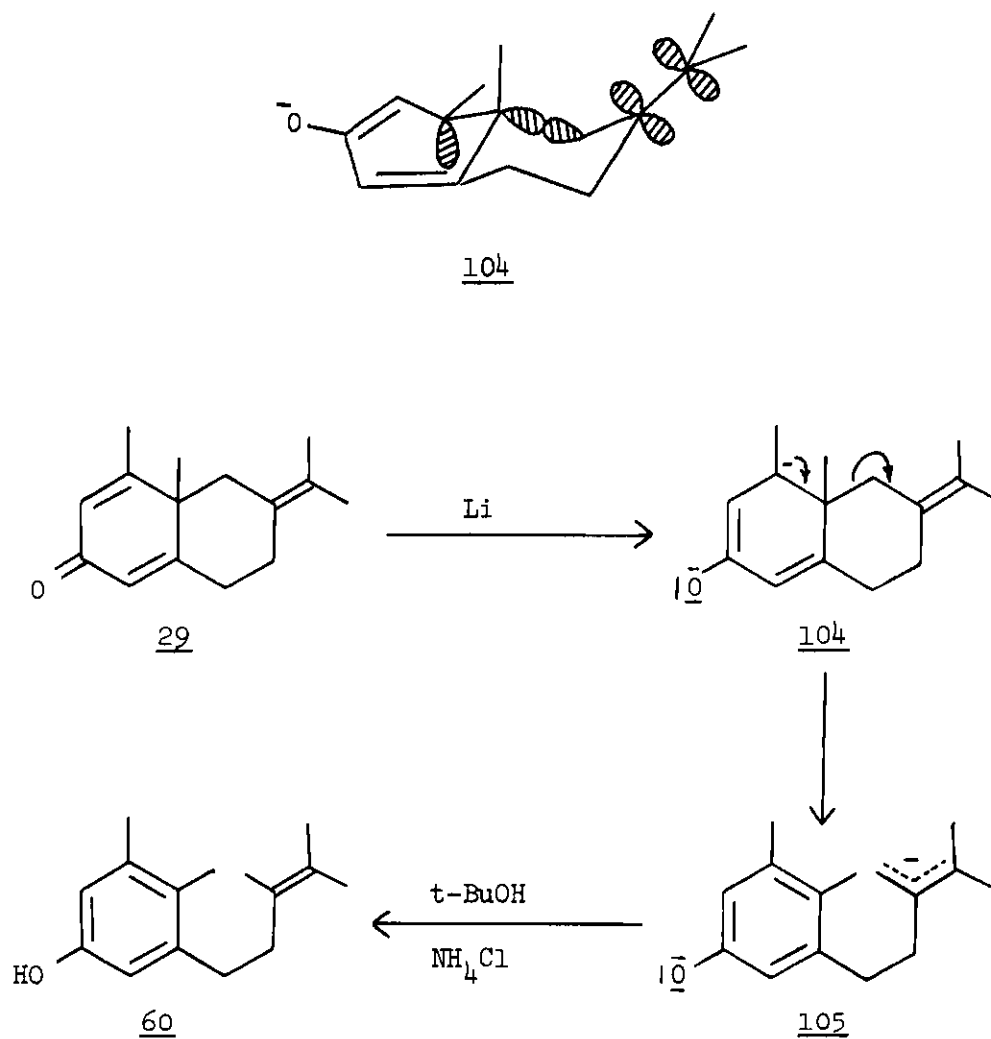


Chart 17. Reduction of Trienone 29 with Lithium in Ammonia

product, while hydroxy ketone 110 was dehydrated with boron tribluoride etherate-acetic acid to give 111, 112 and 113 (Chart 19). His original idea was to find the 1,2 methyl migration in these reactions. Examination of the models of 108 and 110 revealed that the methyl group is antiparallel to the hydroxy group and 1,2-methyl migration was expected.

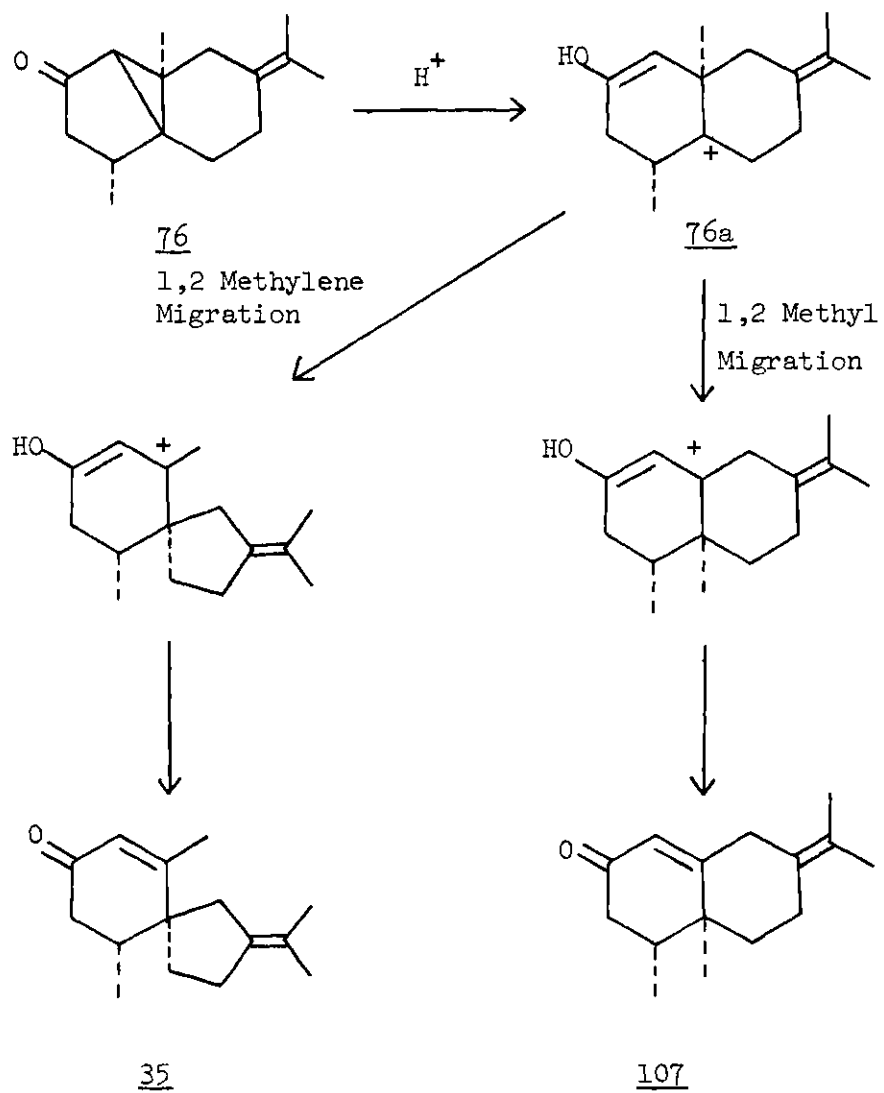


Chart 18. Proposed Acid-Catalyzed Rearrangements of Bicyclo[3.1.0]Hexanone

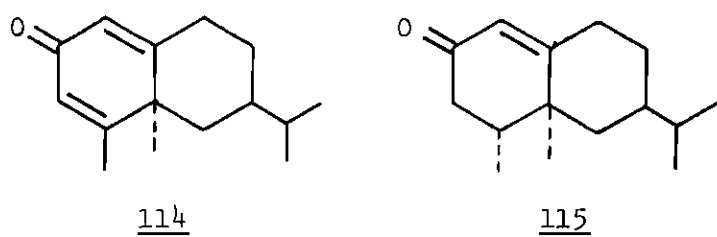
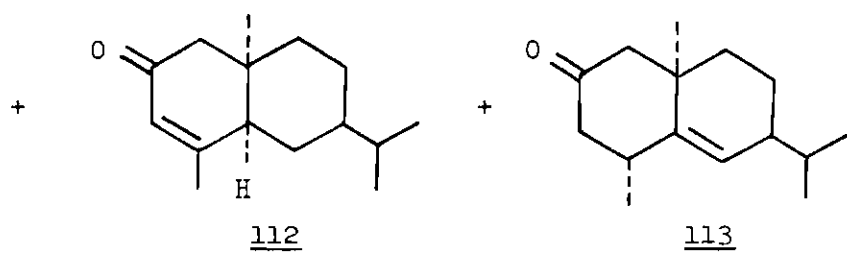
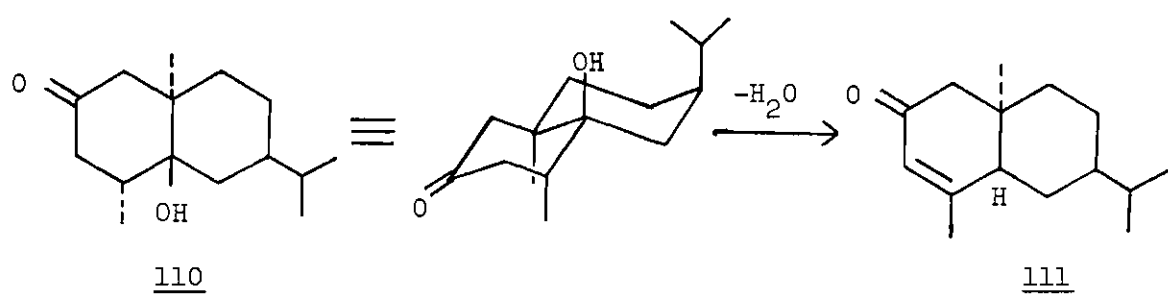
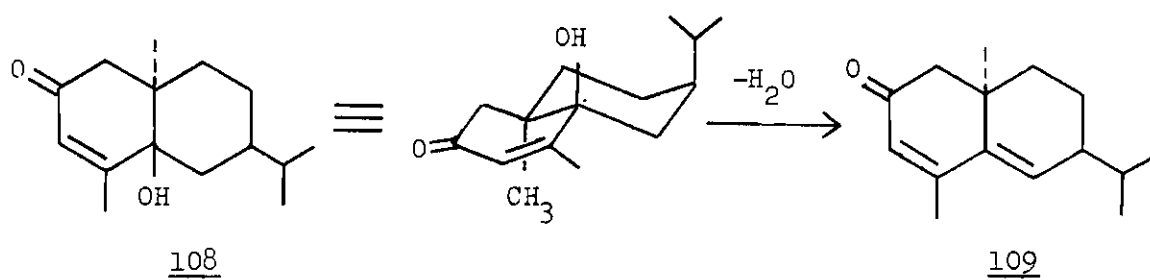


Chart 19. Dehydrations of Bicyclic Alcohols Carried out by Huffman

However, no products like 114 or 115 were isolated in these reactions showing that loss of a proton to form an olefinic bond was the more favorable process.

It seemed that since the enolized form of the carbonyl group is produced when cleavage of the 1,8a-bond occurs to intermediate 76a, the direct formation of the α,β -unsaturated ketone system might provide a driving force for the migration of an alkyl group being competitive with simple proton loss to form an alkene.

Before a study of 76 was undertaken, it was decided that examination of the acid-catalyzed cleavage of several model compounds would be of interest. The starting materials for this study were 47, 48 and 49 which were obtained by catalytic reductions of the corresponding lumiproductions 62, 53 and 66 (Chart 20). The latter compounds were obtained by irradiation of the corresponding dienones 61, 52 and 65, respectively.

The compound 47 was found to be a colorless oil and showed identical spectral properties with those reported (39) previously. The compound 48 was also found to be a colorless oil which was the only product isolated in the hydrogenation of 53. This is because of the steric hindrance on the α side which prevented the formation of the isomer having the 4-methyl group β . The nmr spectrum of 53 showed an angular methyl group at 1.28 ppm and a secondary methyl group at δ 1.14 ($J = 6.5$ Hz) while the ir absorption at 1719 cm^{-1} agreed with the existence of a carbonyl group conjugated with a cyclopropyl ring. It should be noted that 48 has the same structure as 76 except for the

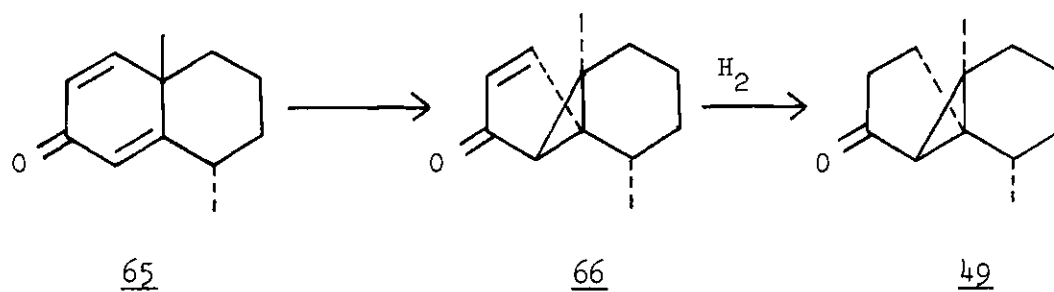
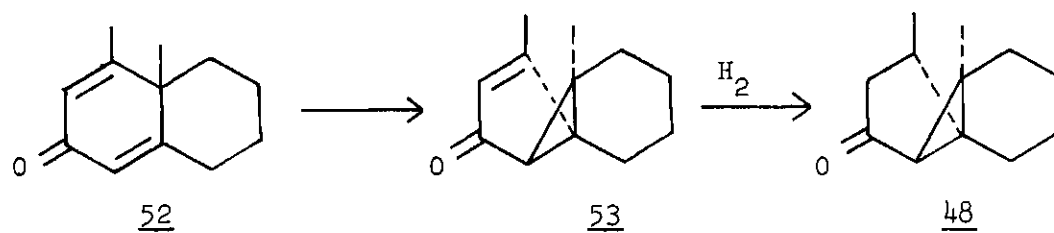
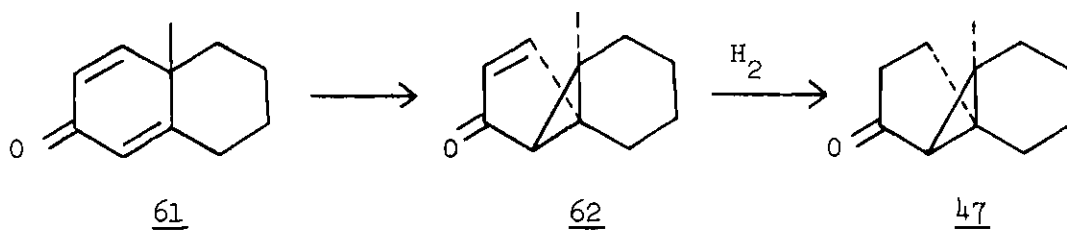


Chart 20. Synthesis of Dihydrolumipproducts 47, 48 and 49

presence of the cyclopropylidene group in the latter. Compound 49 was found to be a colorless oil and was identical with the compound reported by McCurry (40) and by Chao (45) by comparison of their spectral properties.

The hydrobromination and dehydrobromination reactions of 47, 48 and 49 were studied in detail (Chart 21). The reaction of hydrogen bromide with 47 yielded the bromo ketone 69. This structure was assigned on the basis of its nmr spectrum which gave a singlet methyl peak at δ 1.81. This relatively low field position is indicative of the presence of a bromine atom on the carbon bearing the methyl group. The infrared absorption at 1747 cm^{-1} supported the presence of a cyclopentanone ring. Thermodynamic elimination of hydrogen bromide from 69 with tetra-*n*-butylammonium bromide in acetone containing 2,6-lutidine (23) gave a major product which was isolated by preparative glc (22) and assigned the enone structure 70. The nmr spectrum showed a single vinyl methyl group absorption at 1.67 ppm and a single vinyl hydrogen absorption at δ 5.48. The infrared absorption at 1737 cm^{-1} also supported the structure assigned.

The reaction of hydrogen bromide with 48 gave a similar bromo ketone 67. Its nmr spectrum also supported this structure with a downfield methyl group absorption at δ 1.89 and a secondary methyl group absorption at δ 1.31 ($J = 7\text{ Hz}$). Thermodynamic elimination (23) of hydrogen bromide gave a product assigned the structure 68 which showed absorption for a vinyl methyl group and a secondary methyl group in its nmr spectrum and also a cyclopentanone carbonyl absorption in its infrared spectrum. The spectral properties of 70 and 68 were

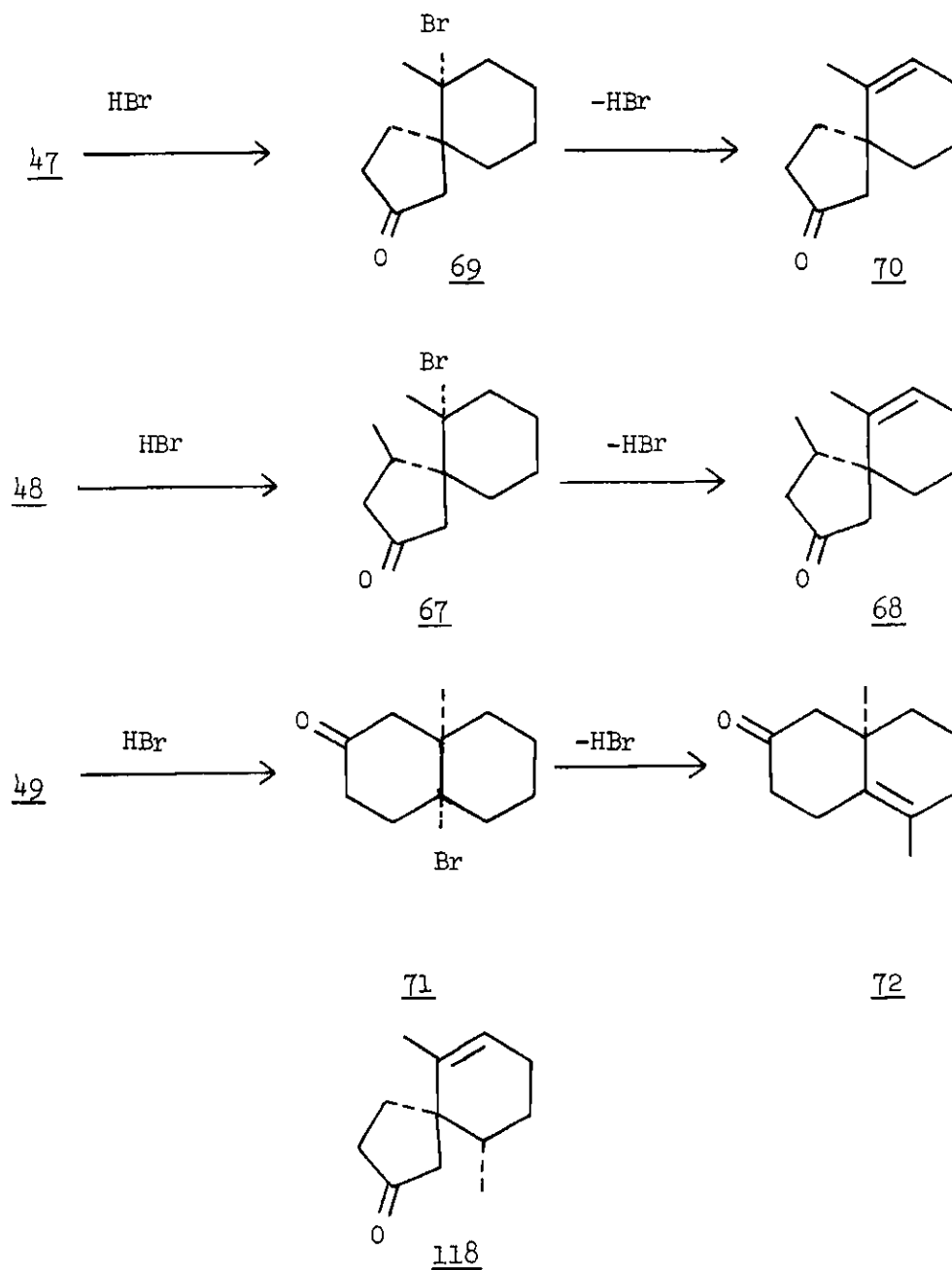


Chart 21. Ring Opening Reactions of 47, 48 and 49 with Hydrogen Bromide Followed by Dehydrobromination of the Product

similar to those of 118 (45) with the appropriate changes for the presence and location of the secondary methyl group being taken into account.

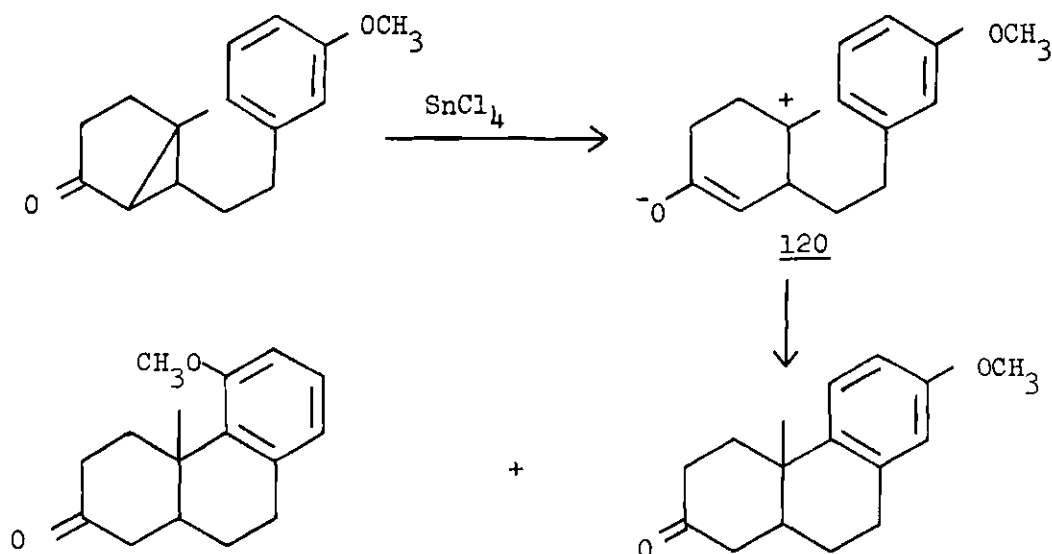
The addition of hydrogen bromide to 49 gave a different type of compound with a singlet methyl group absorption at much higher field (1.15 ppm) in the nmr spectrum. The infrared absorption at 1720 cm^{-1} indicated the presence of a saturated ketone in a six-membered ring. The structure was assigned as 71. Elimination of hydrogen bromide gave a product which showed no vinyl hydrogen absorption in the nmr spectrum and an infrared absorption characteristic of a cyclohexanone. The structure of 72 was assigned to the elimination product. This material exhibited identical spectral properties with those reported by Marshall and coworkers (36).

In the ring opening with hydrogen bromide an S_N-2 -type process with a concerted cleavage of the cyclopropane ring and attack of the bromide ion at the β position being involved is proposed. While the present work provides no direct evidence for the stereochemistry of the bromo ketones 69, 67 and 71, previous work on related steroidal systems (41, 42) indicates that inversion of configuration at the β position would be expected to be involved.

Examination of models of compounds 67, 69 and 71 reveals that the 1,4a-bond of the three membered ring is in a much better position to overlap with the π -orbital of the carbonyl group than the 1,8a-bond. This is borne out by the results of metal-ammonia reduction of compounds of this type which leads to exclusive cleavage of the 1,4a-bond (43).

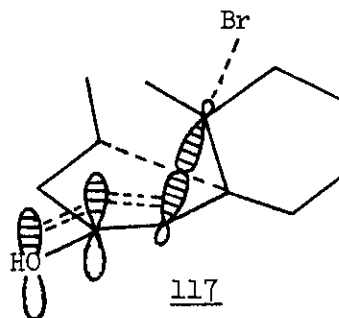
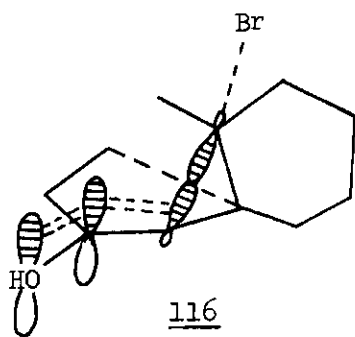
Thus on electronic grounds acid-catalyzed cleavage of the 1,4a-bond with the formation of spiro ketones might be expected to be favored. It should be noted that a tertiary carbonium ion would be produced by cleavage of either the 1,4a- or the 1,8a-bond. The work of Stork et al. has shown that bond cleavage to generate a more stable carbonium ion 120 may be more important than orbital overlap in controlling cleavage of cyclopropyl ketones (44).

However, it appears that the mode of cleavage may be influenced by steric factors associated with approach of the bromide ion to the β position and possibly by steric factors in the developing product.

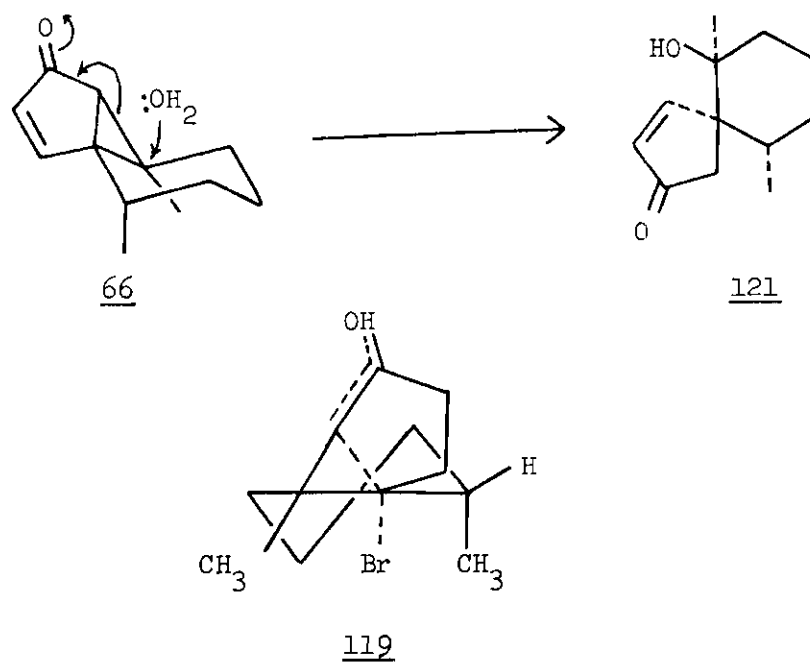
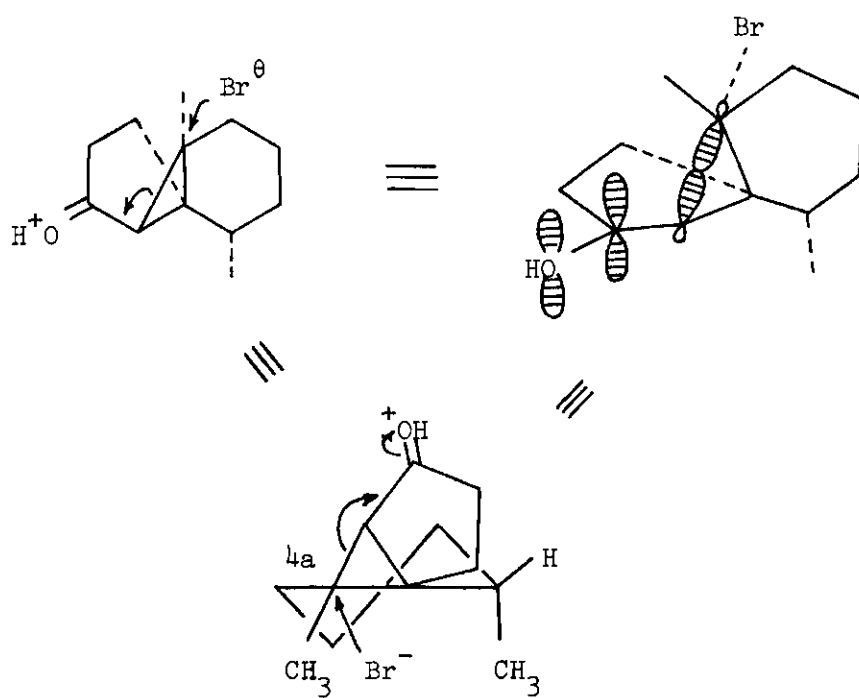


The mode of cleavage of 47 and 48 appears to involve transition states of the type 116 and 117 respectively. In these cases there is favorable orbital overlap between the protonated carbonyl function and the 1,4a-bond and the back side of the 4a carbon atom is not particularly

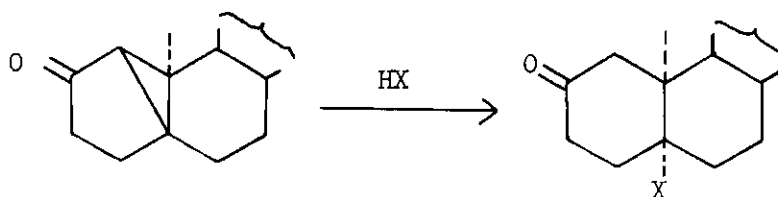
hindered.



For the compound 49 there appears to be hindrance for the bromide ion to approach from the back side of position 4a. The more favorable conformation of the six-membered ring in 49 appears to be the one having the 8-methyl group in the axial orientation. In the conformation having the 8-methyl group equatorial eclipsing between this group and the methylene groups of the five-membered ring is quite severe. If the 8-methyl group is axial, transition state 119 would be involved in the formation of a spiro ketone analogous to 69 and 67. However, in this case a 1,3-diaxial interaction between the 8-methyl group and the attacking bromide ion would occur as was found in the photolysis of 66 (46). In this case the isolation of the front side attack product 121 was probably due to the same hindrance to backside attack. Apparently this transition state is less favorable than transition state 119 which leads to 71, and involves a 1,2-interaction between the 8-methyl group and the attacking bromide ion.



In reactions of steroid compounds with hydrogen halides, attack of halide ion at C-5 (analogous to 8a in the simple tricyclic systems) is generally preferred (41, 42). In these cases, the existence of C/D ring system appears to hinder back side attack at C-10.



Acid-catalyzed reactions of 48 and 49 with the Lewis acid boron trifluoride in ether and in benzene were investigated next. Treatment of 48 with boron trifluoride etherate in benzene at 65°C gave only one major product which was found to be identical with the compound 50. This product could be derived from either bond 1,8a-cleavage of 1,4a-cleavage. The 1,8a-cleavage process would involve a carbonium ion intermediate 122 and a 1,2-methyl migration could yield 50. The 1,4a-cleavage process would lead to the carbonium ion intermediate 123. Then, a 1,2-migration of C-4 would give 50 (Chart 22). In view of the behavior of 48 toward hydrogen bromide it would seem that the latter process involving 1,4-bond cleavage would be the most likely. However, an attempt to convert the spiro enone 68 into 50 under the same reaction conditions was unsuccessful. Thus if the intermediate 123 is involved it appears to undergo rearrangement more rapidly than proton lost to give 68 or its enol.

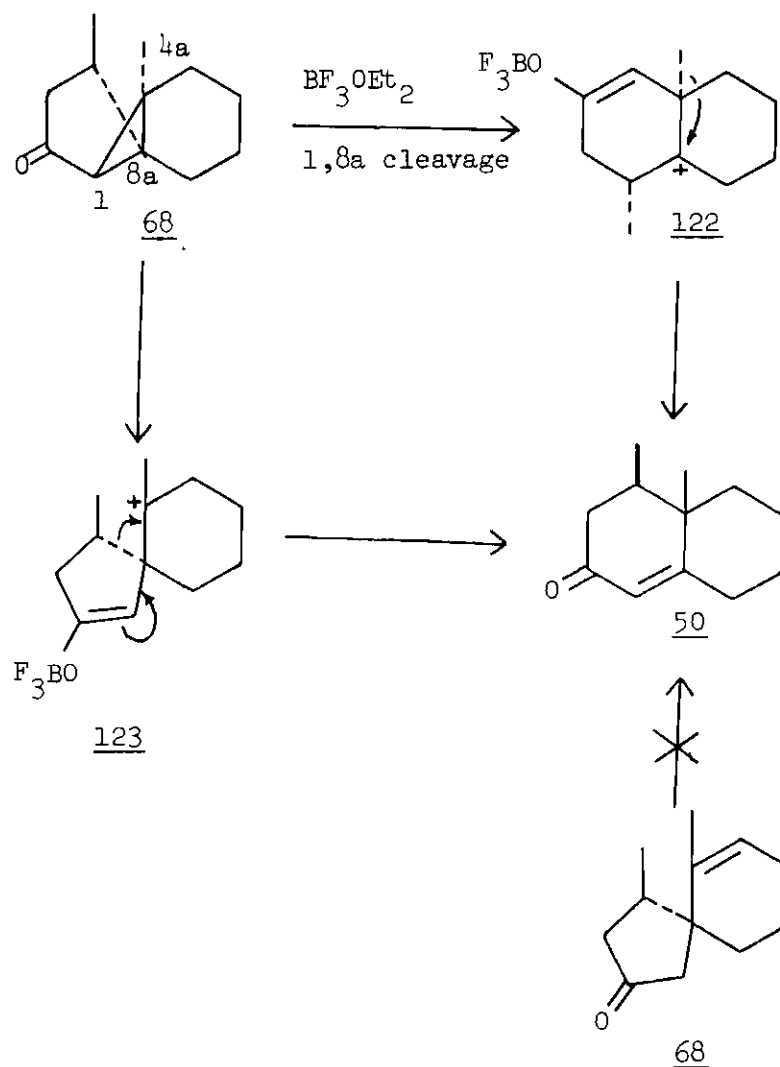


Chart 22. Possible Pathways for the Reaction of 48 with Boron Trifluoride Etherate

In order to distinguish between the two possible pathways, compound 49 was designed to be treated with boron trifluoride etherate under the same condition as 48. Theoretically the two possible ring cleavage processes would lead to different products (Chart 23) and this would determine which pathway was involved in the rearrangement of 48.

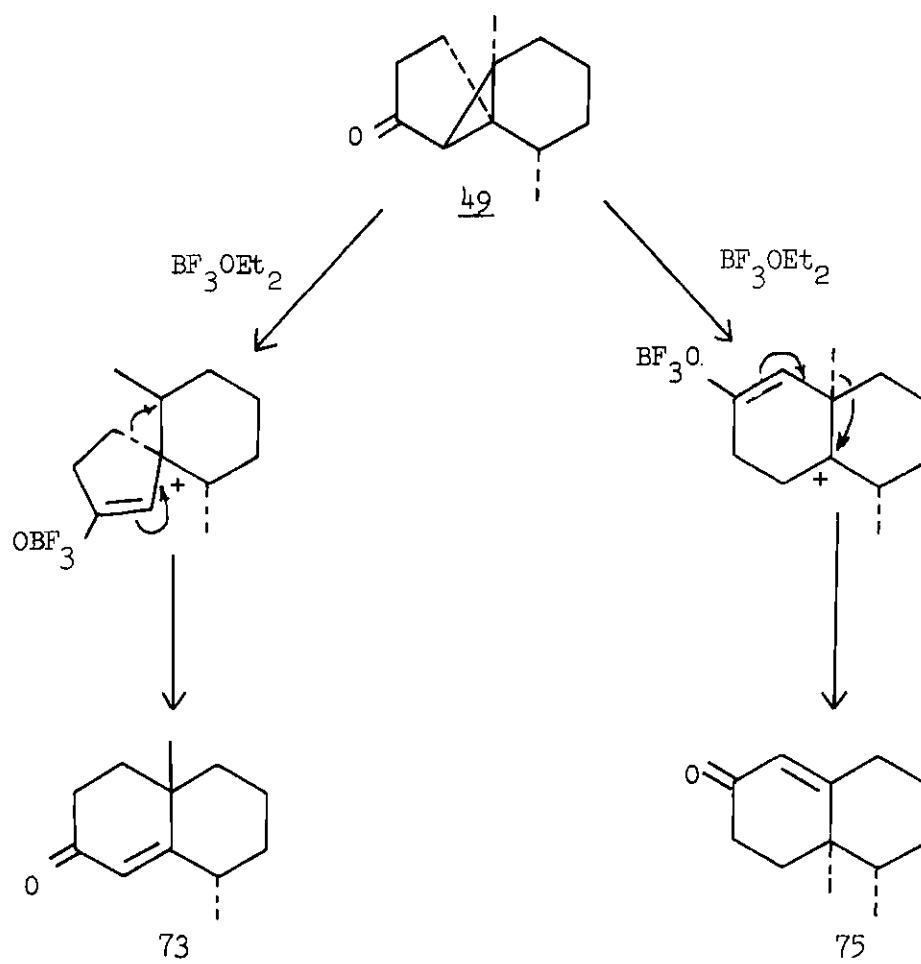
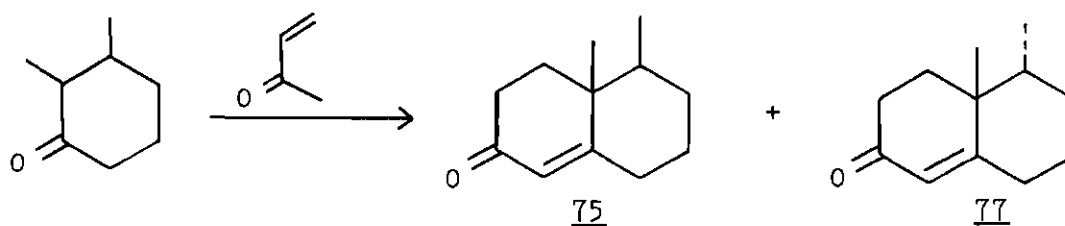


Chart 23. Proposed Acid Ring Opening Reaction of 49 with Boron Trifluoride Etherate

In fact, this reaction was found to give four products in a ratio of 1:5:4:10 in the order of retention times by glc (19) (Chart 24). Yields of the four were determined to be 3, 13, 10 and 26 percent respectively by using benzophenone as internal standard. Two more runs with different conditions were performed. The second run employed a higher ratio of boron trifluoride etherate to substrate (10:3) and in

the third run the more polar solvent ether was employed instead of benzene. For the second run, a product mixture with the same four products in a ratio of 3:3:6:8 was found by glc. Yields were determined in the same way to be 10, 10, 20 and 26 percent respectively. For the third run, the composition of the product was found to be a mixture of the same four compounds in a ratio of 9:2:4:5 by glc. Yields were again in the same way to be 31, 7, 15 and 18 percent respectively. The separation was achieved by collecting through a preparative glc column (22). The first product in the order of glc retention time was found identical with compound 72 by comparison of their spectral properties. The second compound was found to be identical with the compound 73 obtained before and reported by Marshall (36) by comparison of their spectral properties. The third compound was assigned structure 74 according to its spectral properties with the nmr spectrum having one methyl group absorption at δ 1.18, one secondary methyl absorption at δ 0.79 as doublet ($J = 6.5$ Hz) and a vinyl hydrogen absorption at δ 5.38. The infrared spectrum indicated an unconjugated six-membered ring ketone absorption at 1713 cm^{-1} ; and the correct exact mass determination. The last product was found to be identical with 75 which was synthesized independently from 2,3-dimethylcyclohexanone and methyl vinyl ketone as major product by comparing their spectral properties.



In the study of the product composition, it was found that the combination of compounds 72, 74 and 75 made up more than 75 percent of the product in all conditions, while compound 73 consisted of less than 25 percent of it. This strongly suggested that for the compound 49 both the 1,4a and 1,8a bond cleavage processes were involved and that the latter was the most important process. These cleavages would produce carbonium ions 106 and 128 as intermediates. The carbonium ion 128 could undergo a rearrangement to give compound 73 as was proposed in the case 123 to 50 whereas carbonium 106 could undergo either a methyl migration to give compound 75 or simply lose a proton from the C-4 or C-5 position to give compounds 74 and/or 72 (Chart 24). The reason that more compound 72 was isolated as product in the third run using ether as solvent was probably due to the fact that in the more polar media proton transfers were more rapid and the product from proton loss forms faster than the product from methyl migration. Compound 72 and 75 were treated with boron trifluoride etherate under the same conditions as were employed for the reaction of 49 and found to undergo no apparent reaction. This suggested that these products were formed kinetically under the reaction conditions. Although this is no proof

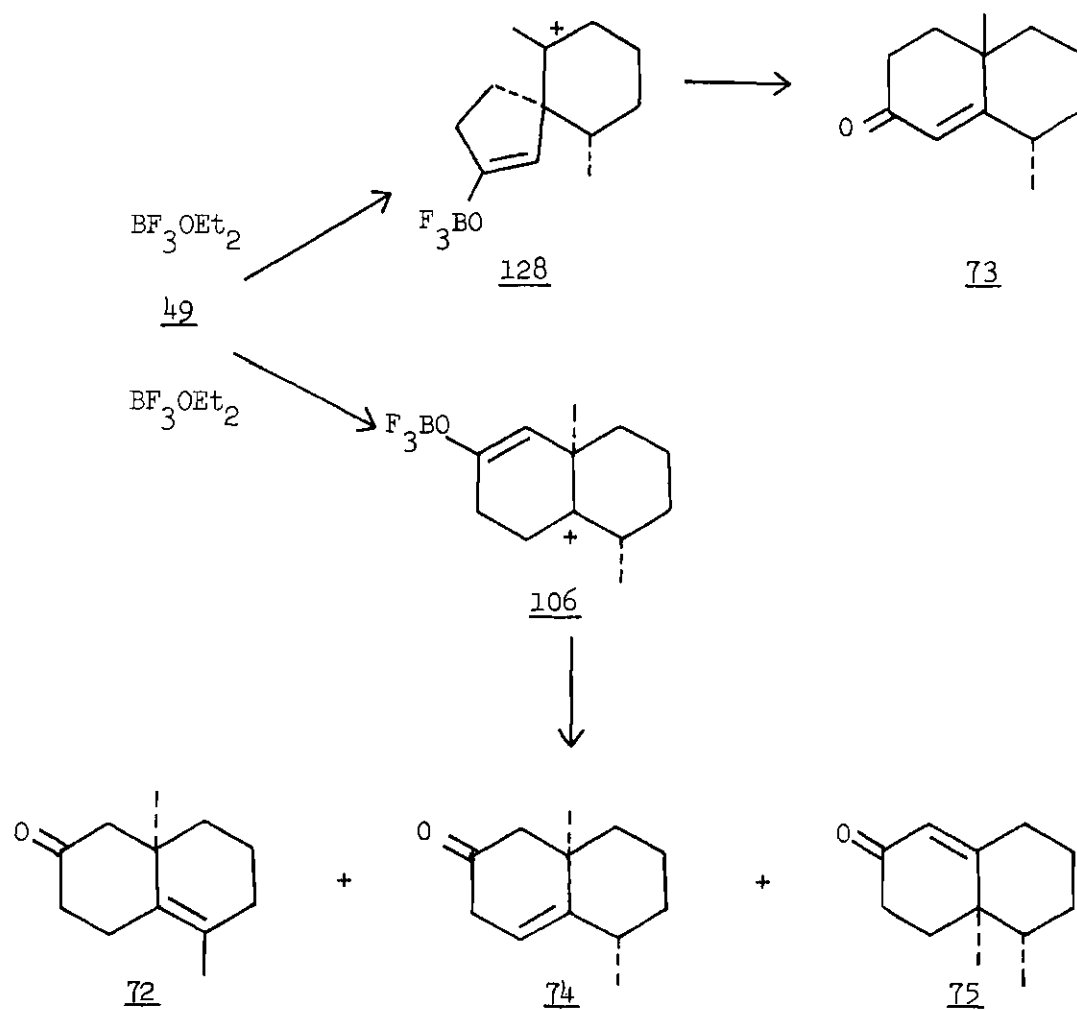
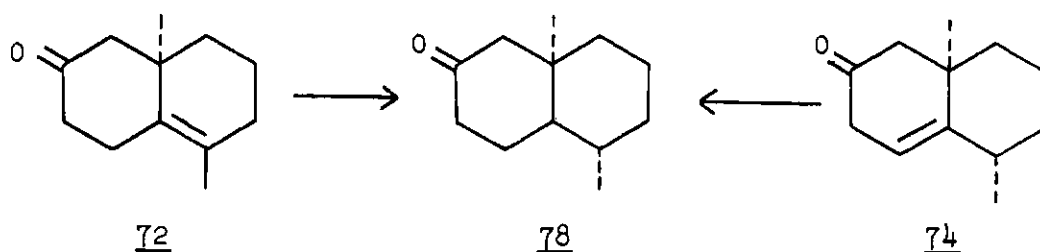


Chart 24. Acid Ring Opening Reaction of 49 with Boron Trifluoride Etherate

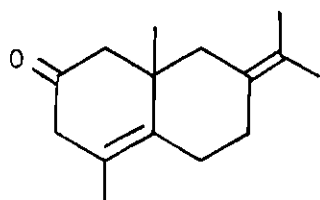
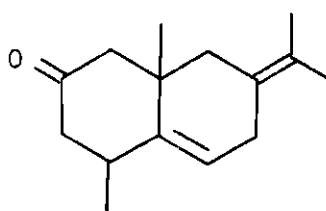
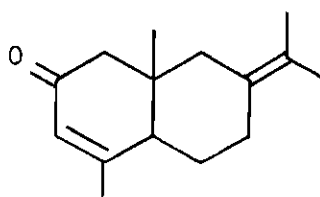
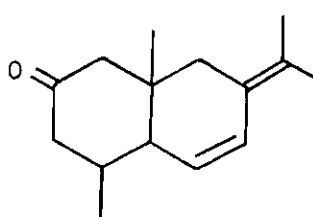
of which process was involved in the reaction of compound 48. The process involving the spiro carbonium ion 123 is favored because of the consistency of the direction of the ring opening toward either hydrogen bromide or boron trifluoride etherate was found in 49 and likely in 48.

The structures of compounds 72 and 74 were further approved by catalytic hydrogenation each compound to give the same product 78 which was supported by its spectral properties glc behavior (19) and exact mass determination.



The dihydrolumipproduct 76 was obtained by catalytic hydrogenation of 33. According to the analysis of glc (19) and the spectral properties, compound 76 was the only product of the reaction. Its nmr spectrum which gave one angular methyl group absorption, one secondary methyl group absorption and two vinyl methyl group absorptions along with an absorption at 1717 cm^{-1} in the ir spectrum also supported the structure assigned. As stated before, the acid-catalyzed ring opening reaction of 76 with boron trifluoride etherate was designed theoretically to give 35 through a 1,2-methylene shift from carbonium ion 76a or 107 through a 1,2-methyl shift (Chart 18). Actually it was found that a mixture of at least six products existed in glc analysis (19),

but none of them corresponded to 35 by comparing their glc retention times. The attempted separation of these compounds were not successful. But similar to compound 49, the product was expected to be a mixture of compound 107 which could be derived from a 1,2-methyl shift and several other products which could be derived from losing a hydrogen from carbonium ion 76a, such as 124, 125 or further rearranged dienones such as 126, 127 et al.

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CHAPTER V

CONCLUSION

In this research, several interesting and important results were found. The C-4 methyl substituted octalones such as 30, 50 and 51 were converted into the corresponding cross-conjugated dienones by oxidation with DDQ. Yields were found to be around 30 to 40 percent in each case. The irradiation of dienones 29, 32, 52 and 61 was found to give the corresponding lumiproducs very efficiently by using a low-pressure light source and in dioxane as solvent. Spiro compounds 34, 38, 54 and 63 were isolated and characterized via irradiation of their corresponding lumiproducs with broad spectrum lamp and in 45 percent aqueous acetic acid as solvent. Pyrex filtered UV light was used in these irradiation and the use of long wave length light is the most important factor allowing the successful isolation of these spiro compounds.

Naturally occurring nootkatone, having a 6/6-fused skeleton, was converted into racemic β -vetivone and its 10-epimer having spiro [4.5]nonane skeletons. The reverse process was found only partially successful due to the fact that the reduction of trienone 29 could not be controlled to produce the desired compound.

In reaction with hydrogen bromide, bicyclo[3.1.0] hexanones 47 and 48 were found to undergo 1,4a-bond cleavage to give corresponding spiro bromo ketones 69 and 67 while compound 49 was found to undergo

1,8a-bond cleavage to give the bicyclic bromo ketone 71. As S_N-2 mechanism was proposed in these conditions, the better overlap of 1,4a-bond in either 47 or 48 with the carbonyl group appears to account for the selective formation of bromo ketone 69 or 67. Steric hindrance to back side attack at the carbon apparently prevents cleavage of the 1,4a-bond of 49 and accounts for the formation of 71. The thermodynamically more stable enones 70, 68 and 72 were obtained by dehydrohalogenation of bromo ketones 69, 67 and 71, respectively, with tetra-n-butylammonium bromide.

On treatment with boron trifluoride etherate, compound 48 was found to give 50 exclusively. Two possible pathways involving initial formation of carbonium ions 122 and/or 123 were considered to be involved in this reaction. The reaction of 49 with boron trifluoride etherate under the same condition, was found to give a mixture of four products, 72, 73, 74 and 75.

The formation of enone 75 was of special interest since it appears to arise by way of a 1,2-methyl migration in a cation of the type considered to be involved in the biogenetic conversion of endesmane into eremophilane sesquiterpenes.

CHAPTER VI

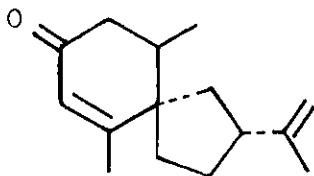
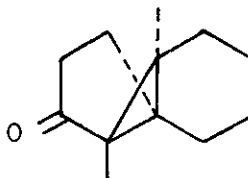
RECOMMENDATIONS

In order to generalize the photolytic rearrangement of cross-conjugated spiro dienones, irradiation of dienones 54 and 63 should be studied. In order to accomplish the study of *in vitro* interconversions of α -vetivone and β -vetivone, further attempts at selective reduction on 1,8a bond of trienone 29 should be made.

Compounds 38 and 129 were found as natural products from a *Solanum* species (31). The attempts of isolation 129 via reduction of 38 should be made.

In addition to the studies of the product mixture from reduction of 34, further attempts to separate β -vetivone and its 10-epimer either by column chromatography or by preparative glc should be made.

In order to compare with the reported steroid analogs and determine the reaction mechanism and substituent effect on acid ring opening reactions, dihydrolumipproducts 130 and 47 should be studied both in strong acid such as hydrogen bromide and in Lewis acid such as boron trifluoride etherate or stannic chloride.

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